Connecting via Winsock to STN

Welcome to STN International! Enter x:x

* * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:17:58 ON 30 APR 2008

=> file react

FILE 'CASREACT' ENTERED AT 11:18:19 ON 30 APR 2008
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'CHEMINFORMRX' ENTERED AT 11:18:19 ON 30 APR 2008
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FILE 'DJSMONLINE' ENTERED AT 11:18:19 ON 30 APR 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION

FILE 'PS' ENTERED AT 11:18:19 ON 30 APR 2008
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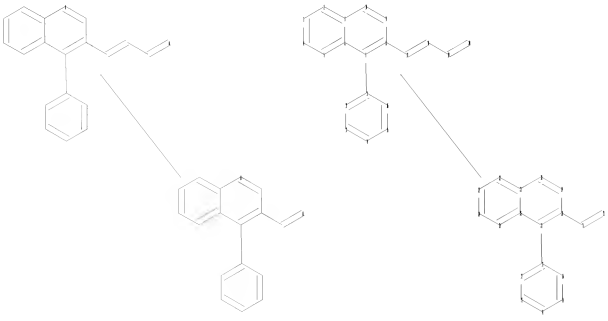
=>
Uploading C:\Program Files\Stnexp\Queries\777.str



chain nodes :
17 18 19 20 37 38
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 21 22 23 24 25 26 27
28 29 30 31 32 33 34 35 36
chain bonds :
7-11 8-17 17-18 18-19 19-20 27-31 28-37 37-38
ring bonds :
1-2 1-6 1-10 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16 21-22 21-26 21-30 22-23 23-24 24-25 25-26 26-27 27-28 28-29
29-30 31-32 31-36 32-33 33-34 34-35 35-36
exact/norm bonds :
19-20 37-38
exact bonds :
7-11 8-17 17-18 18-19 27-31 28-37
normalized bonds :

1-2 1-6 1-10 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16 21-22 21-26 21-30 22-23 23-24 24-25 25-26 26-27 27-28 28-29
29-30 31-32 31-36 32-33 33-34 34-35 35-36

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom
29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom 35:Atom 36:Atom 37:CLASS
38:CLASS
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 21

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 11:18:44 FILE 'CASREACT'
SCREENING COMPLETE - 180 REACTIONS TO VERIFY FROM 16 DOCUMENTS

100.0% DONE 180 VERIFIED 43 HIT RXNS 12 DOCS
SEARCH TIME: 00.00.01

FULL SEARCH INITIATED 11:18:45 FILE 'CHEMINFORMRX'
SCREENING COMPLETE - 27 REACTIONS TO VERIFY FROM 2 DOCUMENTS

100.0% DONE 27 VERIFIED 8 HIT RXNS 1 DOCS
SEARCH TIME: 00.00.04

FULL SEARCH INITIATED 11:18:50 FILE 'DJSMONLINE'
SCREENING COMPLETE - 0 REACTIONS TO VERIFY FROM 0 DOCUMENTS

100.0% DONE 0 VERIFIED 0 HIT RXNS 0 DOCS
SEARCH TIME: 00.00.02

FULL SEARCH INITIATED 11:18:54 FILE 'PS'
SCREENING COMPLETE - 2 REACTIONS TO VERIFY FROM 1 DOCUMENTS

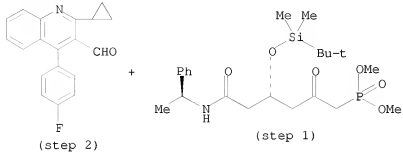
100.0% DONE 2 VERIFIED 2 HIT RXNS 1 DOCS
SEARCH TIME: 00.00.01

L2 14 L1

=
=> d

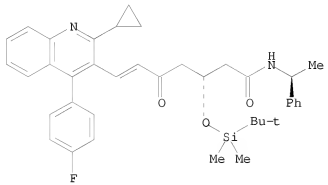
L2 ANSWER 1 OF 14 CASREACT COPYRIGHT 2008 ACS on STN

RX(5) OF 40



1. K2CO3, EtOH
2. EtOH
3. Citric acid, Water

RX(5) OF 40



100%

REF: Helvetica Chimica Acta, 90(6), 1069-1081; 2007
NOTE: stereoselective, Horner-Wadsworth-Emmons reaction
CON: STAGE(1) 0 deg C
STAGE(2) 0 deg C; 0 deg C -> room temperature; 30 minutes,
room temperature; room temperature -> 40 deg C; 48 hours,
40 deg C; 40 deg C -> 45 deg C; 3 hours, 45 deg C
STAGE(3) 45 deg C

=> d ibib abs

L2 ANSWER 1 OF 14 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 147:300962 CASREACT
TITLE: A new and efficient synthesis of the HMG-CoA reductase

inhibitor pitavastatin
AUTHOR(S): Acemoglu, Murat; Brodbeck, Andre; Garcia, Angel; Grimler, Dominique; Hassel, Marc; Riss, Bernhard; Schreiber, Robert
CORPORATE SOURCE: Chemical & Analytical Development, Process Research & Development, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Helvetica Chimica Acta (2007), 90(6), 1069-1081 CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An improved synthetic procedure for the preparation of pitavastatin, calcium 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-(3R,5S,6E)-6-heptenoate, based on asym. ring opening of 3-TBDMSO-glutaric anhydride (1) by chiral amines, is described. Ring opening of 1 in the reaction with (1S)-1-phenylethylamine (R*NH2, 2c) gave the carbamoylbutanoic acid, (3S)-R*NHCOCH2CH(OTBDMS)CH2CO2H (3c), which was converted to Weinreb amide and phosphonylated to give β-oxophosphonate (4S)-R*NHCOCH2CH(OTBDMS)CH2COCH2P(O)(OMe)2 (5) in reaction with LiCH2P(O)(OMe)2. Use of bulkier amines in the asym. ring opening of 1 did not lead to improvement of enantioselectivity. Compound 5 was reacted with 2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinecarboxaldehyde (8) and after stereoselective reduction of the keto-group hydrolyzed to target compound, pitavastatin and its δ-lactone, NK-104. The approach circumvents various synthetic problems associated with the buildup of the 3,5-dihydroxy-C7 acid side chain of HMG-CoA reductase inhibitors (statins). The use of the C6-amide derivative 5 instead of ester derivs. in the coupling reaction with carboxaldehyde 8 prevents undesired elimination and retro-aldol side reactions. The method provides synthetic statins, such as pitavastatin, in > 99% ee and exceptionally high overall yield.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file casreact

=> s l1 full
L3 12 SEA SSS FUL L1 (43 REACTIONS)

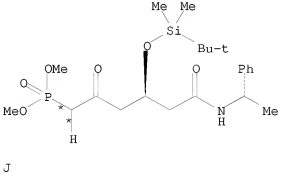
=
ENTER DISPLAY FORMAT (FCRDREF):ibib abs rx

L3 ANSWER 1 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 147:300962 CASREACT
TITLE: A new and efficient synthesis of the HMG-CoA reductase inhibitor pitavastatin
AUTHOR(S): Acemoglu, Murat; Brodbeck, Andre; Garcia, Angel; Grimler, Dominique; Hassel, Marc; Riss, Bernhard; Schreiber, Robert
CORPORATE SOURCE: Chemical & Analytical Development, Process Research & Development, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Helvetica Chimica Acta (2007), 90(6), 1069-1081 CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta

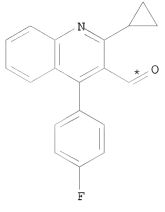
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An improved synthetic procedure for the preparation of pitavastatin, calcium 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-(3R,5S,6E)-6-heptenoate, based on asym. ring opening of 3-TBDMSO-glutaric anhydride (1) by chiral amines, is described. Ring opening of 1 in the reaction with (1S)-1-phenylethylamine (R*NH2, 2c) gave the carbamoylbutanoic acid, (3S)-R*NHCOCH2CH(OTBDMS)CH2CO2H (3c), which was converted to Weinreb amide and phosphonylated to give β-oxophosphonate (4S)-R*NHCOCH2CH(OTBDMS)CH2COCH2P(O)(OMe)2 (5) in reaction with LiCH2P(O)(OMe)2. Use of bulkier amines in the asym. ring opening of 1 did not lead to improvement of enantioselectivity. Compound 5 was reacted with 2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinecarboxaldehyde (8) and after stereoselective reduction of the keto-group hydrolyzed to target compound, pitavastatin and its δ-lactone, NK-104. The approach circumvents various synthetic problems associated with the buildup of the 3,5-dihydroxy-C7 acid side chain of HMG-CoA reductase inhibitors (statins). The use of the C6-amide derivative 5 instead of ester derivs. in the coupling reaction with carboxaldehyde 8 prevents undesired elimination and retro-aldol side reactions. The method provides synthetic statins, such as pitavastatin, in > 99% ee and exceptionally high overall yield.

RX(5) OF 40 ...J + U ===> V...

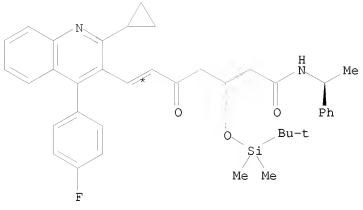


J



U

(5)



V
YIELD 100%

RX(5) RCT J 573690-20-7

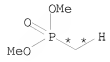
STAGE(1)
RGT W 584-08-7 K2CO3
SOL 64-17-5 EtOH
CON 0 deg C

STAGE(2)
RCT U 121660-37-5
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 30 minutes, room temperature
SUBSTAGE(4) room temperature -> 40 deg C
SUBSTAGE(5) 48 hours, 40 deg C
SUBSTAGE(6) 40 deg C -> 45 deg C
SUBSTAGE(7) 3 hours, 45 deg C

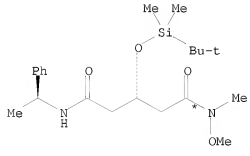
STAGE(3)
RGT X 77-92-9 Citric acid
SOL 7732-18-5 Water
CON 45 deg C

PRO V 573690-21-8
NTE stereoselective, Horner-Wadsworth-Emmons reaction

RX(13) OF 40 COMPOSED OF RX(2), RX(5)
RX(13) H + I + U ===> V



H



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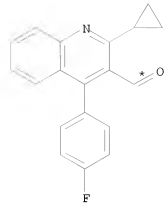
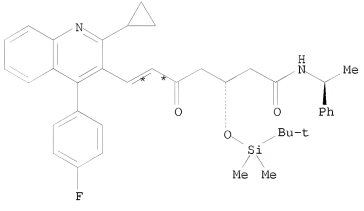


U

2
STEPS

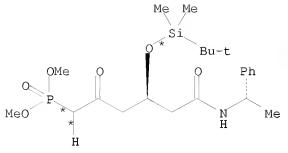


V
YIELD 100%

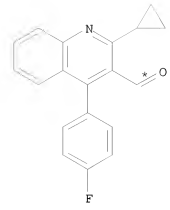
RX(2) RCT H 756-79-6

STAGE(1)
RGT K 109-72-8 BuLi
SOL 109-99-9 THF, 110-54-3 Hexane
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 60 minutes, -78 deg C

```
            STAGE(2)
               RCT  I 573690-18-3
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) 2.5 hours, -78 deg C

            STAGE(3)
               RGT  L 64-19-7 AcOH
               SOL  7732-18-5 Water, 109-99-9 THF
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) -78 deg C -> room temperature

          PRO  J 573690-20-7

RX(5)     RCT  J 573690-20-7

            STAGE(1)
               RGT  W 584-08-7 K2CO3
               SOL  64-17-5 EtOH
               CON  0 deg C

            STAGE(2)
               RCT  U 121660-37-5
               SOL  64-17-5 EtOH
               CON  SUBSTAGE(1) 0 deg C
                    SUBSTAGE(2) 0 deg C -> room temperature
                    SUBSTAGE(3) 30 minutes, room temperature
                    SUBSTAGE(4) room temperature -> 40 deg C
                    SUBSTAGE(5) 48 hours, 40 deg C
                    SUBSTAGE(6) 40 deg C -> 45 deg C
                    SUBSTAGE(7) 3 hours, 45 deg C

            STAGE(3)
               RGT  X 77-92-9 Citric acid
               SOL  7732-18-5 Water
               CON  45 deg C

          PRO  V 573690-21-8
          NTE  stereoselective, Horner-Wadsworth-Emmons reaction


RX(16) OF 40 COMPOSED OF RX(5), RX(6)
RX(16)    J  +  U  ===>  Z
```

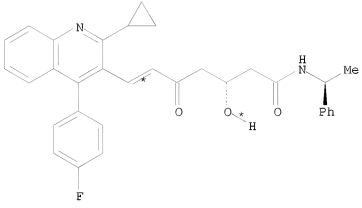


J



U

2
STEPS



Z
YIELD 86%

RX(5) RCT J 573690-20-7

STAGE(1)
RGT W 584-08-7 K2CO3
SOL 64-17-5 EtOH
CON 0 deg C

STAGE(2)
RCT U 121660-37-5
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 30 minutes, room temperature
SUBSTAGE(4) room temperature -> 40 deg C
SUBSTAGE(5) 48 hours, 40 deg C
SUBSTAGE(6) 40 deg C -> 45 deg C

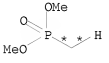
SUBSTAGE(7) 3 hours, 45 deg C

STAGE(3)
RGT X 77-92-9 Citric acid
SOL 7732-18-5 Water
CON 45 deg C

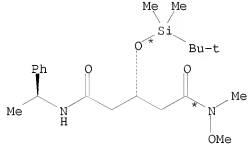
PRO V 573690-21-8
NTE stereoselective, Horner-Wadsworth-Emmons reaction

RX(6) RCT V 573690-21-8
RGT AA 7647-01-0 HCl
PRO Z 573690-23-0
SOL 7732-18-5 Water, 64-17-5 EtOH
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> 25 deg C
SUBSTAGE(3) 4 hours, 25 deg C

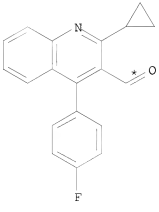
RX(22) OF 40 COMPOSED OF RX(2), RX(5), RX(6)
RX(22) H + I + U ===> Z



H

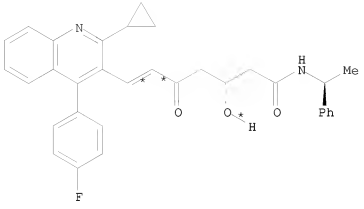


I



U

3
STEPS



Z
YIELD 86%

RX(2) RCT H 756-79-6

STAGE(1)
RGT K 109-72-8 BuLi
SOL 109-99-9 THF, 110-54-3 Hexane
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 60 minutes, -78 deg C

STAGE(2)
RCT I 573690-18-3
SOL 109-99-9 THF
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(3)
RGT L 64-19-7 AcOH
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature

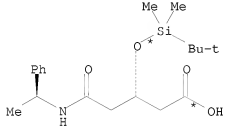
PRO J 573690-20-7

RX(5) RCT J 573690-20-7

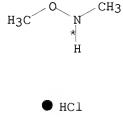
STAGE(1)
RGT W 584-08-7 K2CO3
SOL 64-17-5 EtOH
CON 0 deg C

STAGE(2)
RCT U 121660-37-5
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 30 minutes, room temperature
SUBSTAGE(4) room temperature -> 40 deg C

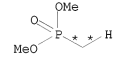
```
                    SUBSTAGE(5) 48 hours, 40 deg C
                    SUBSTAGE(6) 40 deg C -> 45 deg C
                    SUBSTAGE(7) 3 hours, 45 deg C

             STAGE(3)
                RGT  X 77-92-9 Citric acid
                SOL  7732-18-5 Water
                CON  45 deg C

          PRO  V 573690-21-8
          NTE  stereoselective, Horner-Wadsworth-Emmons reaction

RX(6)     RCT  V 573690-21-8
          RGT  AA 7647-01-0 HCl
          PRO  Z 573690-23-0
          SOL  7732-18-5 Water, 64-17-5 EtOH
          CON  SUBSTAGE(1) 0 deg C
               SUBSTAGE(2) 0 deg C -> 25 deg C
               SUBSTAGE(3) 4 hours, 25 deg C


RX(23) OF 40 COMPOSED OF RX(3), RX(2), RX(5), RX(6)
RX(23)    C  +  O  +  H  +  U  ===>  Z
```



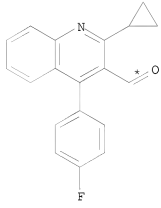
C



O

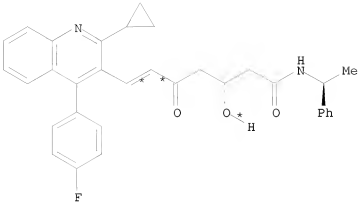


H



U

4
STEPS



Z
YIELD 86%

RX(3) RCT C 121331-22-4

STAGE(1)
RGT P 109-02-4 N-Methylmorpholine
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> -20 deg C

STAGE(2)
RGT Q 543-27-1 ClCO2Bu-i
CON SUBSTAGE(1) -20 deg C
SUBSTAGE(2) 15 minutes, -20 deg C

STAGE(3)
RCT O 6638-79-5
CON SUBSTAGE(1) -20 deg C
SUBSTAGE(2) 1 hour, -20 deg C
SUBSTAGE(3) -20 deg C -> room temperature
SUBSTAGE(4) 4 hours, room temperature

STAGE(4)
RGT G 7732-18-5 Water
CON room temperature

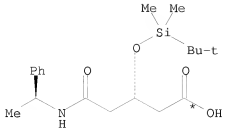
PRO I 573690-18-3

RX(2) RCT H 756-79-6

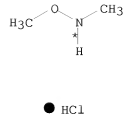
STAGE(1)
RGT K 109-72-8 BuLi
SOL 109-99-9 THF, 110-54-3 Hexane
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 60 minutes, -78 deg C

STAGE(2)

```
                RCT  I 573690-18-3
                SOL  109-99-9 THF
                CON  SUBSTAGE(1) -78 deg C
                     SUBSTAGE(2) 2.5 hours, -78 deg C

             STAGE(3)
                RGT  L 64-19-7 AcOH
                SOL  7732-18-5 Water, 109-99-9 THF
                CON  SUBSTAGE(1) -78 deg C
                     SUBSTAGE(2) -78 deg C -> room temperature

          PRO  J 573690-20-7

RX(5)     RCT  J 573690-20-7

             STAGE(1)
                RGT  W 584-08-7 K2CO3
                SOL  64-17-5 EtOH
                CON  0 deg C

             STAGE(2)
                RCT  U 121660-37-5
                SOL  64-17-5 EtOH
                CON  SUBSTAGE(1) 0 deg C
                     SUBSTAGE(2) 0 deg C -> room temperature
                     SUBSTAGE(3) 30 minutes, room temperature
                     SUBSTAGE(4) room temperature -> 40 deg C
                     SUBSTAGE(5) 48 hours, 40 deg C
                     SUBSTAGE(6) 40 deg C -> 45 deg C
                     SUBSTAGE(7) 3 hours, 45 deg C

             STAGE(3)
                RGT  X 77-92-9 Citric acid
                SOL  7732-18-5 Water
                CON  45 deg C

          PRO  V 573690-21-8
          NTE  stereoselective, Horner-Wadsworth-Emmons reaction

RX(6)     RCT  V 573690-21-8
          RGT  AA 7647-01-0 HCl
          PRO  Z 573690-23-0
          SOL  7732-18-5 Water, 64-17-5 EtOH
          CON  SUBSTAGE(1) 0 deg C
               SUBSTAGE(2) 0 deg C -> 25 deg C
               SUBSTAGE(3) 4 hours, 25 deg C


RX(24) OF 40 COMPOSED OF RX(3), RX(2), RX(5)
RX(24)    C  +  O  +  H  +  U  ===>  V
```



C



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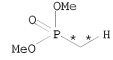

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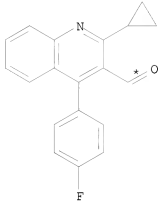
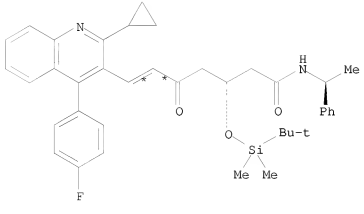


U

3
STEPS

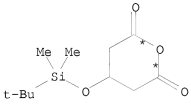


V
YIELD 100%

RX(3) RCT C 121331-22-4

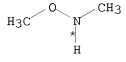
```
            STAGE(1)
               RGT  P 109-02-4 N-Methylmorpholine
               SOL  75-09-2 CH2Cl2
               CON  SUBSTAGE(1) room temperature
                    SUBSTAGE(2) room temperature -> -20 deg C

            STAGE(2)
               RGT  Q 543-27-1 ClCO2Bu-i
               CON  SUBSTAGE(1) -20 deg C
                    SUBSTAGE(2) 15 minutes, -20 deg C

            STAGE(3)
               RCT  O 6638-79-5
               CON  SUBSTAGE(1) -20 deg C
                    SUBSTAGE(2) 1 hour, -20 deg C
                    SUBSTAGE(3) -20 deg C -> room temperature
                    SUBSTAGE(4) 4 hours, room temperature

            STAGE(4)
               RGT  G 7732-18-5 Water
               CON  room temperature

         PRO  I 573690-18-3

RX(2)    RCT  H 756-79-6

            STAGE(1)
               RGT  K 109-72-8 BuLi
               SOL  109-99-9 THF, 110-54-3 Hexane
               CON  SUBSTAGE(1) 3 hours, -78 deg C
                    SUBSTAGE(2) 60 minutes, -78 deg C

            STAGE(2)
               RCT  I 573690-18-3
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) 2.5 hours, -78 deg C

            STAGE(3)
               RGT  L 64-19-7 AcOH
               SOL  7732-18-5 Water, 109-99-9 THF
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) -78 deg C -> room temperature

         PRO  J 573690-20-7

RX(5)    RCT  J 573690-20-7

            STAGE(1)
               RGT  W 584-08-7 K2CO3
               SOL  64-17-5 EtOH
               CON  0 deg C

            STAGE(2)
               RCT  U 121660-37-5
               SOL  64-17-5 EtOH
```

```
          CON  SUBSTAGE(1) 0 deg C
               SUBSTAGE(2) 0 deg C -> room temperature
               SUBSTAGE(3) 30 minutes, room temperature
               SUBSTAGE(4) room temperature -> 40 deg C
               SUBSTAGE(5) 48 hours, 40 deg C
               SUBSTAGE(6) 40 deg C -> 45 deg C
               SUBSTAGE(7) 3 hours, 45 deg C

       STAGE(3)
          RGT  X 77-92-9 Citric acid
          SOL  7732-18-5 Water
          CON  45 deg C

     PRO  V 573690-21-8
     NTE  stereoselective, Horner-Wadsworth-Emmons reaction


RX(25) OF 40 COMPOSED OF RX(1), RX(3), RX(2), RX(5)
RX(25)    A  +  B  +  O  +  H  +  U  ===>  V
```



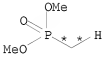
A

B

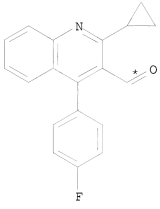


● HCl

O

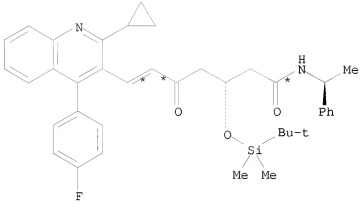


H



U

4
STEPS



V
YIELD 100%

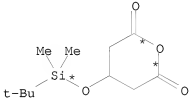
RX(1) RCT A 91424-40-7, B 2627-86-3

STAGE(1)
SOL 142-82-5 Heptane, 1634-04-4 t-BuOMe
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) 60 - 90 minutes, -78 deg C
SUBSTAGE(3) 2 hours, -78 deg C
SUBSTAGE(4) -78 deg C -> 20 deg C

STAGE(2)
RGT D 7664-38-2 H3PO4
SOL 7732-18-5 Water
CON SUBSTAGE(1) 20 deg C -> 35 deg C, pH 2.5 - 3.5
SUBSTAGE(2) 35 deg C -> reflux
SUBSTAGE(3) 30 minutes, reflux
SUBSTAGE(4) reflux -> 0 deg C

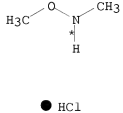
```
          PRO  C 121331-22-4
          NTE  stereoselective

RX(3)     RCT  C 121331-22-4

            STAGE(1)
               RGT  P 109-02-4 N-Methylmorpholine
               SOL  75-09-2 CH2Cl2
               CON  SUBSTAGE(1) room temperature
                    SUBSTAGE(2) room temperature -> -20 deg C

            STAGE(2)
               RGT  Q 543-27-1 ClCO2Bu-i
               CON  SUBSTAGE(1) -20 deg C
                    SUBSTAGE(2) 15 minutes, -20 deg C

            STAGE(3)
               RCT  O 6638-79-5
               CON  SUBSTAGE(1) -20 deg C
                    SUBSTAGE(2) 1 hour, -20 deg C
                    SUBSTAGE(3) -20 deg C -> room temperature
                    SUBSTAGE(4) 4 hours, room temperature

            STAGE(4)
               RGT  G 7732-18-5 Water
               CON  room temperature

          PRO  I 573690-18-3

RX(2)     RCT  H 756-79-6

            STAGE(1)
               RGT  K 109-72-8 BuLi
               SOL  109-99-9 THF, 110-54-3 Hexane
               CON  SUBSTAGE(1) 3 hours, -78 deg C
                    SUBSTAGE(2) 60 minutes, -78 deg C

            STAGE(2)
               RCT  I 573690-18-3
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) 2.5 hours, -78 deg C

            STAGE(3)
               RGT  L 64-19-7 AcOH
               SOL  7732-18-5 Water, 109-99-9 THF
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) -78 deg C -> room temperature

          PRO  J 573690-20-7

RX(5)     RCT  J 573690-20-7

            STAGE(1)
               RGT  W 584-08-7 K2CO3
               SOL  64-17-5 EtOH
```

```
            CON  0 deg C

         STAGE(2)
            RCT  U 121660-37-5
            SOL  64-17-5 EtOH
            CON  SUBSTAGE(1) 0 deg C
                 SUBSTAGE(2) 0 deg C -> room temperature
                 SUBSTAGE(3) 30 minutes, room temperature
                 SUBSTAGE(4) room temperature -> 40 deg C
                 SUBSTAGE(5) 48 hours, 40 deg C
                 SUBSTAGE(6) 40 deg C -> 45 deg C
                 SUBSTAGE(7) 3 hours, 45 deg C

         STAGE(3)
            RGT  X 77-92-9 Citric acid
            SOL  7732-18-5 Water
            CON  45 deg C

      PRO  V 573690-21-8
      NTE  stereoselective, Horner-Wadsworth-Emmons reaction

RX(32) OF 40 COMPOSED OF RX(1), RX(3), RX(2), RX(5), RX(6)
RX(32)    A  +  B  +  O  +  H  +  U  ===>  Z
```



A

B



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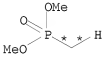
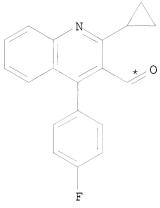
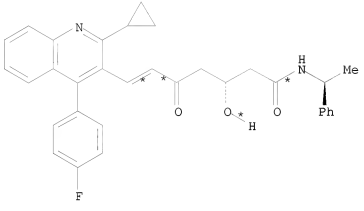


H



U

5
STEPS



Z
YIELD 86%

RX(1) RCT A 91424-40-7, B 2627-86-3

STAGE(1)
SOL 142-82-5 Heptane, 1634-04-4 t-BuOMe
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) 60 - 90 minutes, -78 deg C
SUBSTAGE(3) 2 hours, -78 deg C
SUBSTAGE(4) -78 deg C -> 20 deg C

STAGE(2)
RGT D 7664-38-2 H3PO4
SOL 7732-18-5 Water
CON SUBSTAGE(1) 20 deg C -> 35 deg C, pH 2.5 - 3.5
SUBSTAGE(2) 35 deg C -> reflux
SUBSTAGE(3) 30 minutes, reflux
SUBSTAGE(4) reflux -> 0 deg C

```
          PRO  C 121331-22-4
          NTE  stereoselective

RX(3)     RCT  C 121331-22-4

            STAGE(1)
               RGT  P 109-02-4 N-Methylmorpholine
               SOL  75-09-2 CH2Cl2
               CON  SUBSTAGE(1) room temperature
                    SUBSTAGE(2) room temperature -> -20 deg C

            STAGE(2)
               RGT  Q 543-27-1 ClCO2Bu-i
               CON  SUBSTAGE(1) -20 deg C
                    SUBSTAGE(2) 15 minutes, -20 deg C

            STAGE(3)
               RCT  O 6638-79-5
               CON  SUBSTAGE(1) -20 deg C
                    SUBSTAGE(2) 1 hour, -20 deg C
                    SUBSTAGE(3) -20 deg C -> room temperature
                    SUBSTAGE(4) 4 hours, room temperature

            STAGE(4)
               RGT  G 7732-18-5 Water
               CON  room temperature

          PRO  I 573690-18-3

RX(2)     RCT  H 756-79-6

            STAGE(1)
               RGT  K 109-72-8 BuLi
               SOL  109-99-9 THF, 110-54-3 Hexane
               CON  SUBSTAGE(1) 3 hours, -78 deg C
                    SUBSTAGE(2) 60 minutes, -78 deg C

            STAGE(2)
               RCT  I 573690-18-3
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) 2.5 hours, -78 deg C

            STAGE(3)
               RGT  L 64-19-7 AcOH
               SOL  7732-18-5 Water, 109-99-9 THF
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) -78 deg C -> room temperature

          PRO  J 573690-20-7

RX(5)     RCT  J 573690-20-7

            STAGE(1)
               RGT  W 584-08-7 K2CO3
               SOL  64-17-5 EtOH
```

CON 0 deg C

STAGE(2)
RCT U 121660-37-5
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 30 minutes, room temperature
SUBSTAGE(4) room temperature -> 40 deg C
SUBSTAGE(5) 48 hours, 40 deg C
SUBSTAGE(6) 40 deg C -> 45 deg C
SUBSTAGE(7) 3 hours, 45 deg C

STAGE(3)
RGT X 77-92-9 Citric acid
SOL 7732-18-5 Water
CON 45 deg C

PRO V 573690-21-8
NTE stereoselective, Horner-Wadsworth-Emmons reaction

RX(6) RCT V 573690-21-8
RGT AA 7647-01-0 HCl
PRO Z 573690-23-0
SOL 7732-18-5 Water, 64-17-5 EtOH
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> 25 deg C
SUBSTAGE(3) 4 hours, 25 deg C

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

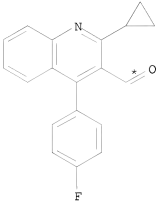
L3 ANSWER 2 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 146:100564 CASREACT
TITLE: Preparation of Pitavastatin calcium with high optical purity as HMG-CoA reductase inhibitor
INVENTOR(S): Wu, Hao; Hu, Guoping; Du, Xiaoxing; Li, Ge
PATENT ASSIGNEE(S): Shanghai Pharmatech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 14pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1876633	A	20061213	CN 2005-10026641	20050610

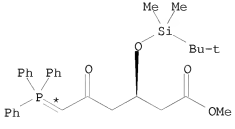
PRIORITY APPLN. INFO.: CN 2005-10026641 20050610
OTHER SOURCE(S): MARPAT 146:100564
AB In this invention, Pitavastatin calcium is prepared from 2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-carbaldehyde with (3R)-3-alkylsiloxoxane-5-carbonyl-6-triphenylphosphoric heptenoate via Wittig reaction to form (E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-

quinoline]-5-carbonyl-(3R)-3-alkylsiloxoxane-6-heptenoate, then deprotection of the alkylsilyl group to obtain (E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinoline]-5-carbonyl-(3R)-hydroxy-6-heptenoate, further selective reduction with NaBH4 or KBH4 in the presence of ligand in a mixed solvents of alc. and ether to give (E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinoline]-(3R,5S)-dihydroxy-6-heptenoate, after hydrolysis with a base to obtain Pitavastatin calcium. Pitavastatin calcium is mainly used as HMG-CoA reductase inhibitor (a hypolipidemic drug).

RX(1) OF 18 A + B ===> C...

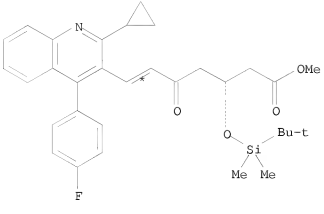


A



B

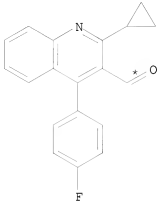
(1)



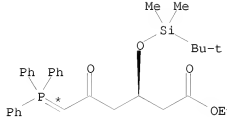
C
YIELD 90%

RX(1) RCT A 121660-37-5, B 147118-35-2
PRO C 182075-76-9
SOL 75-05-8 MeCN
CON 24 hours, 70 - 80 deg C
NTE stereoselective, Wittig reaction

RX(6) OF 18 A + S ===> T

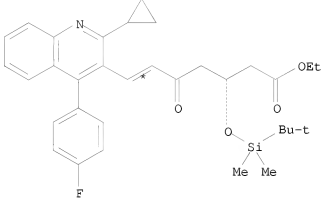


A



S

(6)

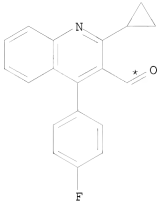


T

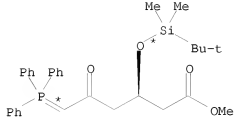
YIELD 85%

RX(6) RCT A 121660-37-5, S 917752-46-6
PRO T 917752-47-7
SOL 108-88-3 PhMe
CON 12 hours, room temperature -> 100 deg C
NTE stereoselective, Wittig reaction, other conditions gave lower yield

RX(9) OF 18 COMPOSED OF RX(1), RX(2)
RX(9) A + B ===> E

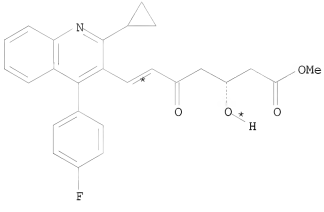


A



B

2 STEPS



E
YIELD 77%

RX(1) RCT A 121660-37-5, B 147118-35-2
PRO C 182075-76-9
SOL 75-05-8 MeCN
CON 24 hours, 70 - 80 deg C
NTE stereoselective, Wittig reaction

RX(2) RCT C 182075-76-9

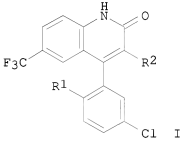
STAGE(1)
RGT F 7664-39-3 HF
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 10 - 24 hours, room temperature
SUBSTAGE(2) cooled

STAGE(2)
RGT G 144-55-8 NaHCO3

SOL 7732-18-5 Water
CON pH 7 - 8

PRO E 917752-45-5

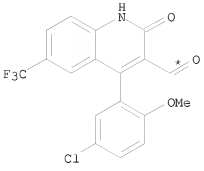
L3 ANSWER 3 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 139:133450 CASREACT
TITLE: 4-Aryl-3-(hydroxyalkyl)quinolin-2-ones: Novel Maxi-K Channel Opening Relaxants of Corporal Smooth Muscle Targeted for Erectile Dysfunction
AUTHOR(S): Hewawasam, Piyasena; Fan, Wenhong; Ding, Min; Flint, Kim; Cook, Deborah; Goggins, Gregory D.; Myers, Robert A.; Gribkoff, Valentin K.; Boissard, Christopher G.; Dworetzky, Steven I.; Starrett, John E., Jr.; Lodge, Nicholas J.
CORPORATE SOURCE: Departments of Chemistry and Neuroscience/Genitourinary Drug Discovery, Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT, 06492, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(14), 2819-2822
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



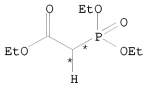
I

AB Novel 4-aryl-3-(hydroxyalkyl)quinoline-2-ones I [R1 = HO, MeO; R2 = HO(CH2)n, n = 1 - 3; R2 = (E)-HOCH2CH:CH] were prepared and evaluated as openers of the cloned maxi-K channel hSlo expressed in Xenopus laevis oocytes by utilizing electrophysiol. methods. The effect of these maxi-K openers on corporal smooth muscle was studied in vitro using isolated rabbit corpus cavernosum. A potent maxi-K opener was identified as an effective relaxant of rabbit corporal smooth muscle and shown to be active in an in vivo animal model of male erectile function.

RX(23) OF 140 ...AL + AP ===> AQ...

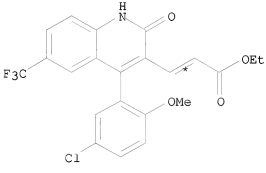


AL



AP

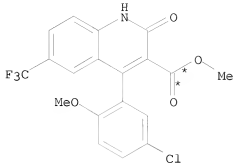
(23)



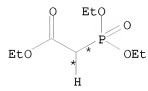
AQ
YIELD 86%

RX(23) RCT AL 275375-53-6, AP 867-13-0
        RGT AR 7646-69-7 NaH
        PRO AQ 275375-54-7
        SOL 68-12-2 DMF

RX(94) OF 140 COMPOSED OF RX(19), RX(20), RX(23)
RX(94) X + AP ===> AQ

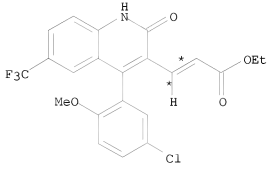


X



AP

3
STEPS



AQ
YIELD 86%

RX(19) RCT X 275375-50-3
RGT AH 13292-87-0 BH3-Me2S
PRO AK 275375-51-4
SOL 109-99-9 THF
CON 23 deg C

RX(20) RCT AK 275375-51-4
RGT AM 1313-13-9 MnO2
PRO AL 275375-53-6
SOL 75-09-2 CH2Cl2
CON 23 deg C

RX(23) RCT AL 275375-53-6, AP 867-13-0
RGT AR 7646-69-7 NaH
PRO AQ 275375-54-7
SOL 68-12-2 DMF

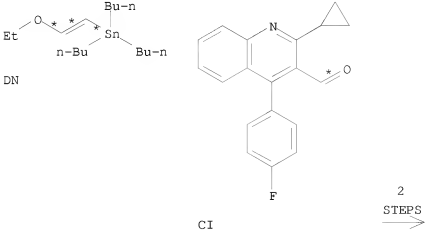
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS

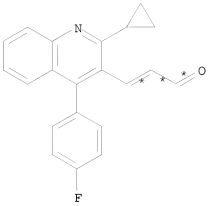
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 136:112193 CASREACT
TITLE: Synthesis and biological evaluations of quinoline-based HMG-CoA reductase inhibitors
AUTHOR(S): Suzuki, M.; Iwasaki, H.; Fujikawa, Y.; Kitahara, M.; Sakashita, M.; Sakoda, R.
CORPORATE SOURCE: Central Research Laboratories, Nissan Chemical Industries, Ltd., Funabashi, Chiba, 274-8507, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(10), 2727-2743
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of quinoline-based 3,5-dihydroxyheptenoic acid derivs. were synthesized from quinolinecarboxylic acid esters by homologation, aldol condensation with Et acetoacetate dianion, and reduction of 3-hydroxyketone to evaluate their ability to inhibit the enzyme HMG-CoA reductase in vitro. In agreement with previous literature, a strict structural requirement exists on the external ring, and 4-fluorophenyl is the most active in this system. For the central ring, substitution on positions 6, 7, and 8 of the central quinoline nucleus moderately affected the potency, whereas the alkyl side chain on the 2-position had a more pronounced influence on activity. Among the derivs., NK-104 (pitavastatin calcium), which has a cyclopropyl group as the alkyl side chain, showed the greatest potency. We found that further modulation and improvement in potency at inhibiting HMG-CoA reductase was obtained by having the optimal substituents flanking the desmethylmevalonic acid portion, i.e., 4-fluorophenyl and cyclopropyl, instead of the usual iso-Pr group.

RX(75) OF 141 COMPOSED OF RX(53), RX(54)
RX(75) DN + CI ===> DS





DS
YIELD 67%

RX(53) RCT DN 20420-43-3

STAGE(1)
RGT DP 109-72-8 BuLi
SOL 109-99-9 THF, 110-54-3 Hexane

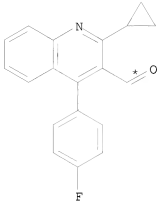
STAGE(2)
RCT CI 121660-37-5
SOL 109-99-9 THF

STAGE(3)
RGT CG 12125-02-9 NH4Cl
SOL 7732-18-5 Water

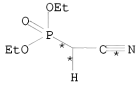
PRO DO 391681-95-1
NTE stereoselective

RX(54) RCT DO 391681-95-1
RGT DT 104-15-4 TsOH
PRO DS 148901-68-2
SOL 109-99-9 THF, 7732-18-5 Water

RX(78) OF 141 COMPOSED OF RX(56), RX(55)
RX(78) CI + DV ===> DS

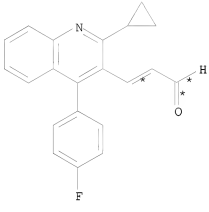


CI



DV

2
STEPS



DS
YIELD 87%

RX(56) RCT CI 121660-37-5, DV 2537-48-6

STAGE(1)
RGT DW 5137-55-3 Capriquat, C 1310-73-2 NaOH
SOL 7732-18-5 Water, 108-88-3 PhMe

STAGE(2)
RGT DX 7647-01-0 HCl
SOL 7732-18-5 Water

PRO DU 256431-72-8
NTE Emmons-Horner reaction, stereoselective

RX(55) RCT DU 256431-72-8

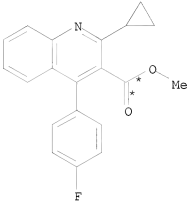
STAGE(1)

RGT CF 1191-15-7 AlH(Bu-i)2
SOL 108-88-3 PhMe

STAGE(2)
RGT D 64-17-5 EtOH

PRO DS 148901-68-2

RX(88) OF 141 COMPOSED OF RX(38), RX(39), RX(53), RX(54)
RX(88) BX + DN ===> DS



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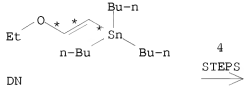
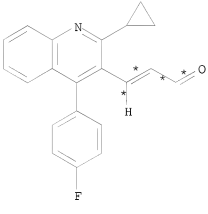


DN

4 STEPS



DS
YIELD 67%

RX(38) RCT BX 121659-86-7

STAGE(1)
RGT CF 1191-15-7 AlH(Bu-i)2

```
                SOL  108-88-3 PhMe

              STAGE(2)
                 RGT  CG 12125-02-9 NH4Cl
                 SOL  7732-18-5 Water

            PRO  CE 121660-11-5

RX(39)      RCT  CE 121660-11-5
            RGT  CJ 26299-14-9 PCC, CK 127-09-3 AcONa
            PRO  CI 121660-37-5
            SOL  75-09-2 CH2Cl2

RX(53)      RCT  DN 20420-43-3

              STAGE(1)
                 RGT  DP 109-72-8 BuLi
                 SOL  109-99-9 THF, 110-54-3 Hexane

              STAGE(2)
                 RCT  CI 121660-37-5
                 SOL  109-99-9 THF

              STAGE(3)
                 RGT  CG 12125-02-9 NH4Cl
                 SOL  7732-18-5 Water

            PRO  DO 391681-95-1
            NTE  stereoselective

RX(54)      RCT  DO 391681-95-1
            RGT  DT 104-15-4 TsOH
            PRO  DS 148901-68-2
            SOL  109-99-9 THF, 7732-18-5 Water


RX(89) OF 141 COMPOSED OF RX(38), RX(39), RX(56), RX(55)
RX(89)      BX  +  DV  ===>  DS
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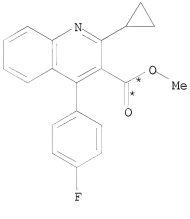
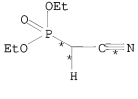
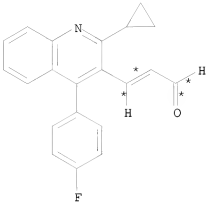




BX DV

4 STEPS



DS
YIELD 87%

RX(38) RCT BX 121659-86-7

STAGE(1)
RGT CF 1191-15-7 AlH(Bu-i)2
SOL 108-88-3 PhMe

STAGE(2)
RGT CG 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO CE 121660-11-5

RX(39) RCT CE 121660-11-5
RGT CJ 26299-14-9 PCC, CK 127-09-3 AcONa
PRO CI 121660-37-5
SOL 75-09-2 CH2Cl2

RX(56) RCT CI 121660-37-5, DV 2537-48-6

STAGE(1)
RGT DW 5137-55-3 Capriquat, C 1310-73-2 NaOH
SOL 7732-18-5 Water, 108-88-3 PhMe

STAGE(2)
RGT DX 7647-01-0 HCl
SOL 7732-18-5 Water

PRO DU 256431-72-8
NTE Emmons-Horner reaction, stereoselective

RX(55) RCT DU 256431-72-8

STAGE(1)
RGT CF 1191-15-7 AlH(Bu-i)2
SOL 108-88-3 PhMe

STAGE(2)
RGT D 64-17-5 EtOH

PRO DS 148901-68-2

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 135:180711 CASREACT
TITLE: Processes for preparing quinoline derivatives and intermediates thereof
INVENTOR(S): Tatsuta, Kuniaki; Kikuyama, Shigeki; Tamai, Yoshin
PATENT ASSIGNEE(S): Kuraray Co., Ltd., Japan; Nissan Chemical Industries, Ltd.
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060800	A1	20010823	WO 2001-JP1184	20010219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001316368	A	20011113	JP 2001-37097	20010214
JP 2001316369	A	20011113	JP 2001-37106	20010214
CA 2400977	A1	20010823	CA 2001-2400977	20010219
AU 2001032342	A	20010827	AU 2001-32342	20010219
EP 1262476	A1	20021204	EP 2001-904553	20010219
EP 1262476	B1	20070110		
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US 6855824	B2	20050215		

PRIORITY APPLN. INFO.: JP 2000-42594 20000221
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WO 2001-JP1184 20010219

OTHER SOURCE(S): MARPAT 135:180711
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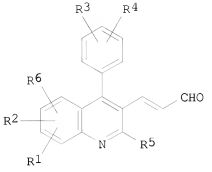

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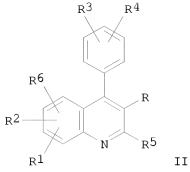
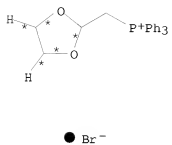


II

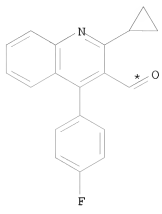
AB A process for preparing quinoline derivs. [I; R1-R6 = H, halo, CF3, CF3O, (un)protected OH, (un)substituted alkyl, cycloalkyl, aryl, aralkyl, alkoxy, or aryloxy] comprises Wittig condensation or Horner-Emmons reaction of a quinolinecarbaldehyde (II; R = CHO; R1-R5) with one member selected from among compds. (R9)3P+CH2CH(OR7)OR8.X- [R7, R8 = H, (un)substituted alkyl, acyl, or aralkyl, or R7 and R8 are joined together to form an alkylene, arylene, or aralkylene; R9 = (un)substituted aralkyl or aryl; X = halo], (R9O)2P(O)CH2CH(OR7)OR8 (R7-R9 = same as above), and (R9O)2P(O)CH:CHNR10R11 [R9 = same as above; R10, R11 = H, (un)substituted alkyl, cycloalkyl, aryl, or aralkyl] in the presence of a base and hydrolyzing the obtained compound The quinolinecarbaldehyde II (R = CHO) are prepared by reduction of quinolinecarboxylic acid esters II [R = CO2R12; R1-R6 = same as above; R12 = (un)substituted alkyl, cycloalkyl, aryl, or aralkyl] with aluminum hydride complex in the presence of a secondary amine. The compound I, e.g. (E)-3-(4-(4-fluorophenyl)-2-cyclopropylquinolin-3-yl)propenaldehyde (III), is useful as an intermediate for quinoline-series mevalonolactone derivative which is known as a HMG-CoA reductase inhibitor in cholesterol biosynthesis. This process is efficient and industrially advantageous since it give I in shorter steps using industrially readily available and easily handled chems. Thus, 4.18 g morpholine was added dropurse slowly to 0.569 g LiAlH4 in 10 mL THF to give the reaction solution which was cooled to 0°, treated dropurse with a solution of 3.21 g Me 4-(4-fluorophenyl)-2-cyclopropylquinoline-3-carboxylate in 9.63 g THF at 0°, and the resulting mixture was stirred at 10-20° for 2 h and treated with 15% aqueous H2SO4 at ≤10° to give, after workup and silica gel chromatog., 77% 4-(4-fluorophenyl)-2-cyclopropylquinoline-3-carbaldehyde (IV). A pentane solution of potassium tert-butoxide (1.51 mL, 2.40 mL) was added dropurse at 20-30° over a period of 2 min to a solution of 1.55 g (1,3-dioxolan-2-ylmethyl)triphenylphosphonium bromide in 10.0 mL anhydrous DMSO, stirred at room temperature for 15 min, treated with a solution of 1.00 g IV in 5 mL anhydrous DMSO at 20-30° over a period of 5 min, and stirred at the same temperature for 90 min. The reaction mixture was treated with 10 mL water followed by separating the organic layer and extracting the water layer with 20 mL hexane twice, and the combined organic layers were washed with water, dried over anhydrous Na2SO4, and concentrated in vacuo. The concentrate residue was dissolved in 20 mL THF, treated with 2 M aqueous HCl, and stirred at room

temperature for 30 min to give, after workup and silica gel chromatog., 90.9% III.

RX(3) OF 11 ...G + B ===> H

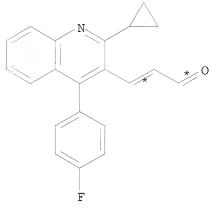


G



B

(3)



H
YIELD 91%

RX(3) RCT G 52509-14-5

STAGE(1)
RGT I 865-47-4 t-BuOK
SOL 67-68-5 DMSO, 109-66-0 Pentane

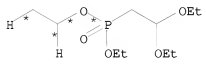
STAGE(2)
RCT B 121660-37-5
SOL 67-68-5 DMSO

STAGE(3)

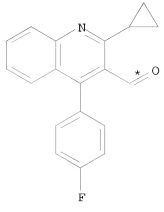
RGT J 7647-01-0 HCl
SOL 109-99-9 THF, 7732-18-5 Water

PRO H 148901-68-2
NTE 20-30° for 2 min and room temp. for 15 min; 20-30° for 95 min; hydrolysis at room temp. for 30 min

RX(4) OF 11 ...N + B ===> H

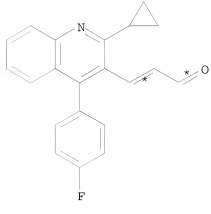


N



B

(4)



H
YIELD 85%

RX(4) RCT N 7598-61-0

STAGE(1)
RGT O 109-72-8 BuLi
SOL 109-99-9 THF, 110-54-3 Hexane

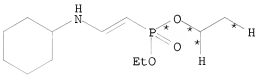
STAGE(2)

RCT B 121660-37-5
SOL 109-99-9 THF

STAGE(3)
RGT P 7601-90-3 HClO4
SOL 7732-18-5 Water, 108-88-3 PhMe

PRO H 148901-68-2
NTE -30° to -20° 65 min; -30° to -20°
for 5 min and room temp. for 2 h; hydrolysis at 40-50°
for 1 h

RX(5) OF 11 ...S + B ===> H



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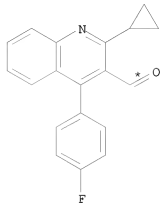
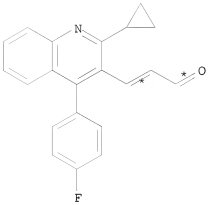


B

(5)



H
YIELD 87%

RX(5) RCT S 20061-84-1

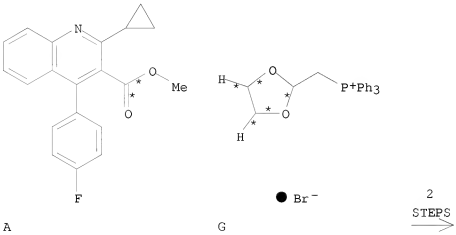
STAGE(1)
RGT T 7646-69-7 NaH
SOL 109-99-9 THF

STAGE(2)
RCT B 121660-37-5
SOL 109-99-9 THF

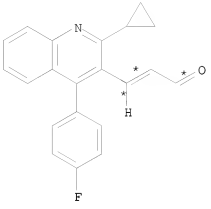
STAGE(3)
RGT U 6153-56-6 Oxalic acid 2H2O
SOL 7732-18-5 Water, 108-88-3 PhMe

PRO H 148901-68-2
NTE -10° to -20° for 65 min; -10° to -5° for 65 min; hydrolysis at 60-70° for 1 h

RX(6) OF 11 COMPOSED OF RX(1), RX(3)
RX(6) A + G ===> H



A G



H
YIELD 91%

RX(1) RCT A 121659-86-7
RGT C 16853-85-3 LiAlH4, D 110-91-8 Morpholine
PRO B 121660-37-5
SOL 109-99-9 THF
NTE 10-20° for 2 h

RX(3) RCT G 52509-14-5

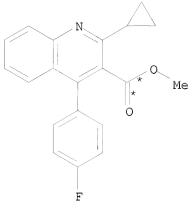
STAGE(1)
RGT I 865-47-4 t-BuOK
SOL 67-68-5 DMSO, 109-66-0 Pentane

STAGE(2)
RCT B 121660-37-5
SOL 67-68-5 DMSO

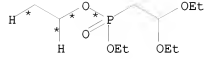
STAGE(3)
RGT J 7647-01-0 HCl
SOL 109-99-9 THF, 7732-18-5 Water

PRO H 148901-68-2
NTE 20-30° for 2 min and room temp. for 15 min; 20-30° for 95 min; hydrolysis at room temp. for 30 min

RX(7) OF 11 COMPOSED OF RX(1), RX(4)
RX(7) A + N ===> H

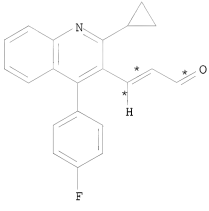


A



N

2
STEPS



H
YIELD 85%

RX(1) RCT A 121659-86-7
RGT C 16853-85-3 LiAlH4, D 110-91-8 Morpholine
PRO B 121660-37-5
SOL 109-99-9 THF
NTE 10-20° for 2 h

RX(4) RCT N 7598-61-0

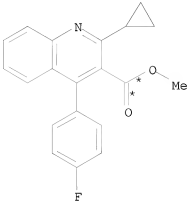
STAGE(1)
RGT O 109-72-8 BuLi
SOL 109-99-9 THF, 110-54-3 Hexane

STAGE(2)
RCT B 121660-37-5
SOL 109-99-9 THF

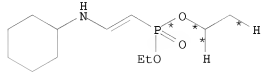
STAGE(3)
RGT P 7601-90-3 HClO4
SOL 7732-18-5 Water, 108-88-3 PhMe

PRO H 148901-68-2
NTE -30° to -20° 65 min; -30° to -20°
for 5 min and room temp. for 2 h; hydrolysis at 40-50°
for 1 h

RX(8) OF 11 COMPOSED OF RX(1), RX(5)
RX(8) A + S ===> H

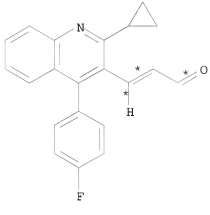


A



S

2
STEPS



H
YIELD 87%

RX(1) RCT A 121659-86-7
RGT C 16853-85-3 LiAlH4, D 110-91-8 Morpholine
PRO B 121660-37-5

SOL 109-99-9 THF
NTE 10-20° for 2 h

RX(5) RCT S 20061-84-1

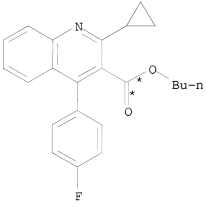
STAGE(1)
RGT T 7646-69-7 NaH
SOL 109-99-9 THF

STAGE(2)
RCT B 121660-37-5
SOL 109-99-9 THF

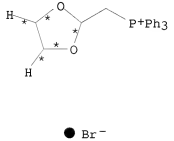
STAGE(3)
RGT U 6153-56-6 Oxalic acid 2H2O
SOL 7732-18-5 Water, 108-88-3 PhMe

PRO H 148901-68-2
NTE -10° to -20° for 65 min; -10° to -5° for 65 min; hydrolysis at 60-70° for 1 h

RX(9) OF 11 COMPOSED OF RX(2), RX(3)
RX(9) F + G ===> H

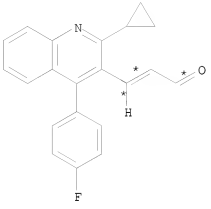


F



G

2 STEPS



H
YIELD 91%

RX(2) RCT F 355804-76-1
RGT C 16853-85-3 LiAlH4, D 110-91-8 Morpholine
PRO B 121660-37-5
SOL 109-99-9 THF
NTE 10-20° for 2 h

RX(3) RCT G 52509-14-5

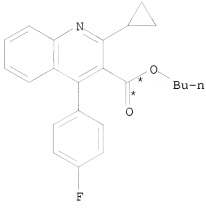
STAGE(1)
RGT I 865-47-4 t-BuOK
SOL 67-68-5 DMSO, 109-66-0 Pentane

STAGE(2)
RCT B 121660-37-5
SOL 67-68-5 DMSO

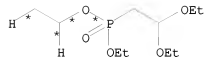
STAGE(3)
RGT J 7647-01-0 HCl
SOL 109-99-9 THF, 7732-18-5 Water

PRO H 148901-68-2
NTE 20-30° for 2 min and room temp. for 15 min; 20-30° for 95 min; hydrolysis at room temp. for 30 min

RX(10) OF 11 COMPOSED OF RX(2), RX(4)
RX(10) F + N ===> H

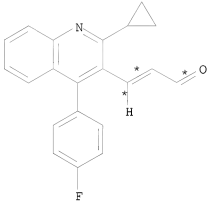


F



N

2
STEPS



H
YIELD 85%

RX(2) RCT F 355804-76-1
RGT C 16853-85-3 LiAlH4, D 110-91-8 Morpholine
PRO B 121660-37-5
SOL 109-99-9 THF
NTE 10-20° for 2 h

RX(4) RCT N 7598-61-0

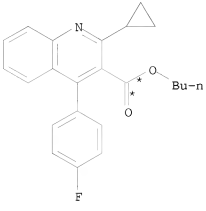
STAGE(1)
RGT O 109-72-8 BuLi
SOL 109-99-9 THF, 110-54-3 Hexane

STAGE(2)
RCT B 121660-37-5
SOL 109-99-9 THF

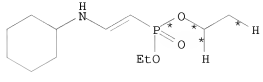
STAGE(3)
RGT P 7601-90-3 HClO4
SOL 7732-18-5 Water, 108-88-3 PhMe

PRO H 148901-68-2
NTE -30° to -20° 65 min; -30° to -20°
for 5 min and room temp. for 2 h; hydrolysis at 40-50°
for 1 h

RX(11) OF 11 COMPOSED OF RX(2), RX(5)
RX(11) F + S ===> H

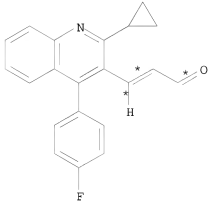


F



S

2
STEPS



H
YIELD 87%

RX(2) RCT F 355804-76-1
RGT C 16853-85-3 LiAlH4, D 110-91-8 Morpholine
PRO B 121660-37-5

SOL 109-99-9 THF
NTE 10-20° for 2 h

RX(5) RCT S 20061-84-1

STAGE(1)
RGT T 7646-69-7 NaH
SOL 109-99-9 THF

STAGE(2)
RCT B 121660-37-5
SOL 109-99-9 THF

STAGE(3)
RGT U 6153-56-6 Oxalic acid 2H2O
SOL 7732-18-5 Water, 108-88-3 PhMe

PRO H 148901-68-2
NTE -10° to -20° for 65 min; -10° to -5° for 65 min; hydrolysis at 60-70° for 1 h

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

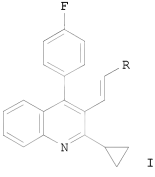
L3 ANSWER 6 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 132:122527 CASREACT
TITLE: Process for the preparation of quinoline derivative and intermediate therefor
INVENTOR(S): Ohara, Yoshio; Suzuki, Mikio; Yanagawa, Yoshinobu; Takada, Yasutaka
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005213	A1	20000203	WO 1999-JP3923	19990722
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338334	A1	20000203	CA 1999-2338334	19990722
AU 9947992	A	20000214	AU 1999-47992	19990722
AU 746722	B2	20020502		
EP 1099694	A1	20010516	EP 1999-931484	19990722
EP 1099694	B1	20050817		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

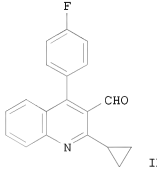
	IE, SI, LT, LV, FI, RO			
NZ 509401	A	20020828	NZ 1999-509401	19990722
CN 1107670	B	20030507	CN 1999-809003	19990722
RU 2214402	C2	20031020	RU 2001-105200	19990722
AT 302190	T	20050915	AT 1999-931484	19990722
PT 1099694	T	20051031	PT 1999-931484	19990722
ES 2247813	T3	20060301	ES 1999-931484	19990722
SK 285675	B6	20070607	SK 2001-62	19990722
ZA 2001000525	A	20010801	ZA 2001-525	20010118
NO 2001000357	A	20010122	NO 2001-357	20010122
NO 317787	B1	20041213		
US 6335449	B1	20020101	US 2001-764994	20010123
MX 2001PA00890	A	20020604	MX 2001-PA890	20010123
			JP 1998-207911	19980723
			WO 1999-JP3923	19990722

PRIORITY APPLN. INFO.:

GI



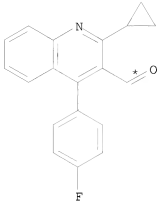
I



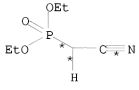
II

AB Claimed is a process for the preparation of 3-quinolinylpropenal derivative (I; R = CHO) through quinolylacrylonitrile I (R = cyano) which can be prepared by reacting quinolinealdehyde (II) with di-Et cyanomethyl phosphonate. I (R = CHO) is useful as an intermediate for a cholesterol-lowering agent (HMG-CoA reductase inhibitor) (III.1/2Ca). Thus, 400 g 20% aqueous NaOH was added dropwise to a mixture of II 199, di-Et cyanomethylphosphonate 136, and Aliquat 336 5.5 g in 960 g PhMe at 25-35° over 0.5-1 h and stirred at the same temperature for 1 h to give, after workup and recrystn. from hexane, 88% I (R = cyano). The latter nitrile (181 g) was dissolved in 1,812 mL PhMe and cooled to -10°, followed by adding a 1.02 M solution of diisobutylaluminum (664 mmol, 650 mL) at -10° to -5° over 1 h, and the resulting mixture was stirred at the same temperature for 1 h to give, after workup and recrystn. from a mixture of cyclohexane and n-hexane, 93% I (R = CHO).

RX(3) OF 3 COMPOSED OF RX(1), RX(2)
RX(3) A + B ===> G

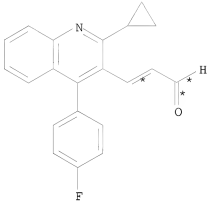


A



B

2
STEPS



G
YIELD 93%

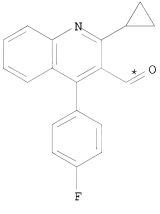
RX(1) RCT A 121660-37-5, B 2537-48-6
RGT D 1310-73-2 NaOH
PRO C 256431-72-8
SOL 7732-18-5 Water, 108-88-3 PhMe
NTE 25-35.DEGREE. FOR 1 H, ALIQUAT 336/CATALYST

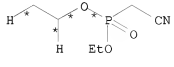
RX(2) RCT C 256431-72-8
RGT H 16853-85-3 LiAlH4
PRO G 148901-68-2
SOL 108-88-3 PhMe
NTE 25-30° for 1 h

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

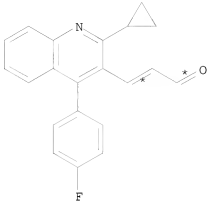
L3 ANSWER 7 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 132:93197 CASREACT
TITLE: First systematic chiral syntheses of two pairs of enantiomers with 3,5-dihydroxyheptenoic acid chain, associated with a potent synthetic statin NK-104
AUTHOR(S): Suzuki, Mikio; Yanagawa, Yoshinobu; Iwasaki, Hiroshi; Kanda, Hiroyasu; Yanagihara, Kazufumi; Matsumoto, Hiroo; Ohara, Yoshio; Yazaki, Yukari; Sakoda, Ryozo
CORPORATE SOURCE: Central Research Institute, Nissan Chemical Industries Ltd., Chiba, 274-8507, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(20), 2977-2982
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB All 4 enantiomers of the synthetic statin NK-104 were prepared The syn diol isomers (NK-104 and its enantiomer) were obtained efficiently by diastereomer resolution The anti diol isomers (3-epimer and 5-epimer) were prepared effectively by asym. aldol reaction followed by anti stereoselective reduction as key steps. Their purity detns. were effected by chiral HPLC anal.

RX(2) OF 46 ...F + G ===> B...





F G (2) →



B

RX(2) RCT F 121660-37-5, G 2537-48-6

STAGE(1)
RGT H 1310-73-2 NaOH
CAT 5137-55-3 Capriquat
SOL 7732-18-5 Water, 108-88-3 PhMe

STAGE(2)
RGT I 1191-15-7 AlH(Bu-i)2

PRO B 148901-68-2
NTE phase-transfer conditions first stage

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 125:248102 CASREACT
TITLE: Preparation of optically active 3-(silyloxy)-5-oxoheptenoic acid ester
INVENTOR(S): Harada, Katsumasa; Matsushita, Akio; Kawachi, Yasuhiro; Sasaki, Hiroshi
PATENT ASSIGNEE(S): Ube Kosan KK, Japan; Nissan Kagaku Kogyo KK; Nissan Chemical Industries, Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08127585	A	19960521	JP 1994-276395	19941110

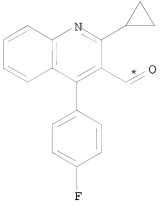
JP 3481325 B2 20031222
PRIORITY APPLN. INFO.: JP 1994-276395 19941110
JP 1994-212960 19940906

GI

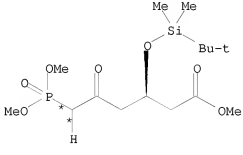
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title ester (I), useful as intermediate for pharmaceuticals, is prepared in high yields by an improved process. K2CO3 was added to a solution of aldehyde II and (R)-III (99% e.e) in 1:1 iso-PrOH-THF containing 0.63% H2O with stirring at room temperature to give 94% (3R,6E)-I of 99% e.e. Also used was MeOH-THF.

RX(1) OF 1 A + B ===> C

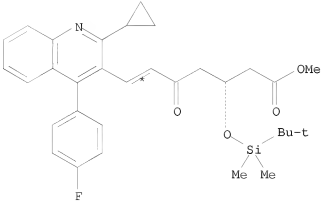


A



B

(1)



C
YIELD 94%

```
RX(1)     RCT  A 121660-37-5, B 96555-58-7
          RGT  D 497-19-8 Na2CO3
          PRO  C 182075-76-9
          SOL  67-63-0 Me2CHOH, 109-99-9 THF
          NTE  99% e.e.
```

```
L3   ANSWER 9 OF 12  CASREACT  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        123:286068  CASREACT
TITLE:                   Preparation of pyrimidine derivatives
INVENTOR(S):             Okada, Tetsuo; Konoike, Toshiro
PATENT ASSIGNEE(S):      Shionogi Seiyaku Kk, Japan
SOURCE:                  Jpn. Kokai Tokkyo Koho, 7 pp.
                         CODEN: JKXXAF
DOCUMENT TYPE:           Patent
LANGUAGE:                Japanese
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
     ---------------  ----  --------      ---------------  --------
     JP 07118233       A    19950509      JP 1993-261365   19931019
     JP 3400038        B2   20030428
PRIORITY APPLN. INFO.:                    JP 1993-261365   19931019
OTHER SOURCE(S):         MARPAT 123:286068
GI
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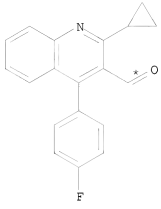
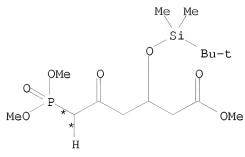
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *
```

AB Pyrimidine derivs. I [R1 = (un)substituted alkyl, etc.; R2, R3 = H, (un)substituted alkyl, etc.; R4 = H, carboxy-protecting group; R5 = H, hydroxy-protecting group; X = N, etc.], useful as pharmaceutical intermediates, are prepared from pyrimidinecarboxaldehydes. Thus, a mixture of pyrimidine derivative II, phosphonate III (TBDMS = tert-butyldimethylsilyl), and potassium tert-butoxide in acetonitrile was stirred at room temperature for 30 min to give, after workup, 74% pyrimidine derivative IV.

```
RX(5) OF 5     O  +  B  ===>  P
```

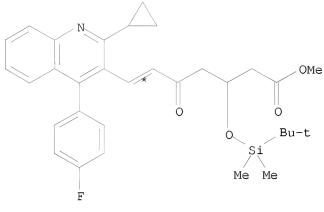


O



B

(5)

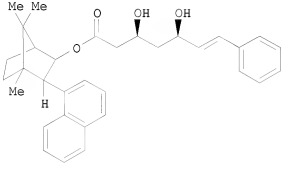


P
YIELD 80%

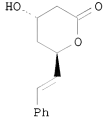
RX(5) RCT O 121660-37-5, B 144149-66-6
RGT H 865-47-4 t-BuOK
PRO P 169196-10-5
SOL 75-05-8 MeCN
NTE 2 h at room temp.

L3 ANSWER 10 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 123:285697 CASREACT
TITLE: Stereoselective reduction of β,δ-diketo esters. A novel strategy for the synthesis of artificial HMG-CoA reductase inhibitors
AUTHOR(S): Hiyama, Tamejiro; Reddy, Guntoori Bhaskar; Minami,

Tatsuya; Hanamoto, Takeshi
CORPORATE SOURCE: Sagami Chemical Research Center, Kanagawa, 229, Japan
SOURCE: Bulletin of the Chemical Society of Japan (1995), 68(1), 350-63
CODEN: BCSJA8; ISSN: 0009-2673
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



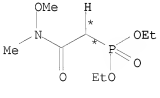
I



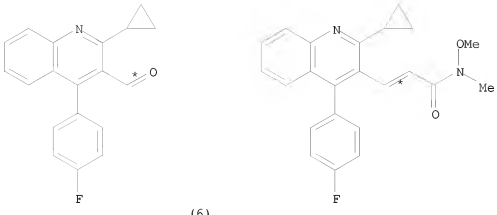
II

AB Condensation of N-methoxy-N-Me amides with acetoacetate dianions gave β,δ-diketo esters, which were selectively reduced with Et2BOMe-NaBH4 in THF/MeOH to give syn-β,δ-dihydroxy esters in one step. Similarly, the β,δ-diketo esters of the Taber's chiral alc. or its enantiomer resp. were reduced to give syn-β,δ-dihydroxy esters of moderate enantiomeric excess. Higher diastereoselective and enantioselectivity were achieved by reduction of the β,δ-diketo esters of Taber's chiral alc. or its enantiomer successively with diisobutylalane and with Et2BOMe-NaBH4. The resulting syn-diol esters were hydrolyzed and lactonized to give various types of β-hydroxy-δ-lactones commonly found in artificial HMG-CoA reductase inhibitors; pharmacol. test data were not shown. The precursor I was converted to the example compound [4S-[4α,6β(E)]]-tetrahydro-4-hydroxy-6-(2-phenylethenyl)-2H-pyran-2-one (II).

RX(6) OF 163 R + S ===> T...



R



S (6) T
YIELD 92%

RX(6) RCT R 124931-12-0

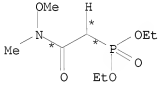
STAGE(1)
RGT U 109-72-8 BuLi
SOL 110-54-3 Hexane, 109-99-9 THF

STAGE(2)
RCT S 121660-37-5
SOL 109-99-9 THF

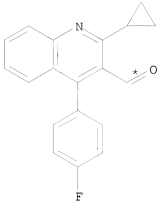
STAGE(3)
RGT I 7732-18-5 Water

PRO T 141750-56-3
NTE alternative prepn. shown, stereoselective

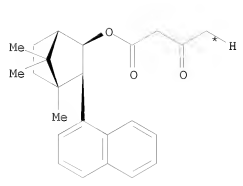
RX(55) OF 163 COMPOSED OF RX(6), RX(38)
RX(55) R + S + BF ===> CM



R

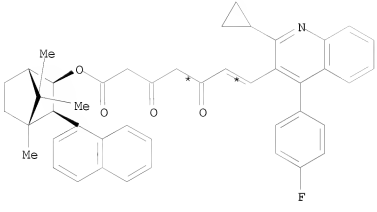


S



BF

2
STEPS



CM
YIELD 48%

RX(6) RCT R 124931-12-0

STAGE(1)
RGT U 109-72-8 BuLi
SOL 110-54-3 Hexane, 109-99-9 THF

STAGE(2)
RCT S 121660-37-5
SOL 109-99-9 THF

STAGE(3)
RGT I 7732-18-5 Water

PRO T 141750-56-3
NTE alternative prepn. shown, stereoselective

RX(38) RCT BF 86835-21-4

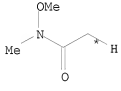
STAGE(1)
RGT AB 7646-69-7 NaH
SOL 109-99-9 THF

STAGE(2)
RGT U 109-72-8 BuLi
SOL 110-54-3 Hexane

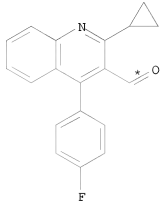
STAGE(3)
RCT T 141750-56-3
SOL 109-99-9 THF

PRO CM 141750-57-4

RX(91) OF 163 COMPOSED OF RX(46), RX(45)
RX(91) CV + S ===> T

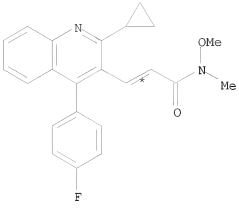


CV



S

2
STEPS



T
YIELD 80%

RX(46) RCT CV 78191-00-1

STAGE(1)
RGT CW 4111-54-0 LiN(Pr-i)2
SOL 110-54-3 Hexane, 109-99-9 THF

STAGE(2)
RCT S 121660-37-5
SOL 109-99-9 THF

STAGE(3)
RGT I 7732-18-5 Water

PRO CS 155849-96-0
NTE in-situ generated reagent

RX(45) RCT CS 155849-96-0

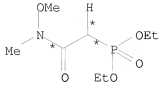
STAGE(1)
RGT CT 124-63-0 MeSO2Cl, CU 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT CU 121-44-8 Et3N

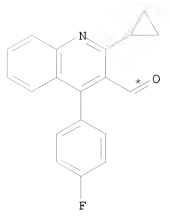
STAGE(3)
RGT AW 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO T 141750-56-3
NTE alternative prepn. shown, stereoselective

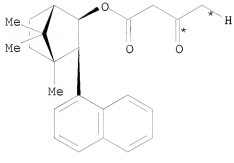
RX(96) OF 163 COMPOSED OF RX(6), RX(38), RX(40)
RX(96) R + S + BF ===> CN



R

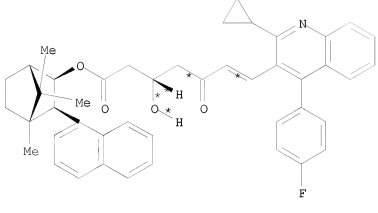


S



BF

3
STEPS



CN
YIELD 56%

```
RX(6)     RCT  R 124931-12-0

            STAGE(1)
              RGT  U 109-72-8 BuLi
              SOL  110-54-3 Hexane, 109-99-9 THF

            STAGE(2)
              RCT  S 121660-37-5
              SOL  109-99-9 THF

            STAGE(3)
              RGT  I 7732-18-5 Water

          PRO  T 141750-56-3
          NTE  alternative prepn. shown, stereoselective

RX(38)    RCT  BF 86835-21-4

            STAGE(1)
              RGT  AB 7646-69-7 NaH
              SOL  109-99-9 THF

            STAGE(2)
              RGT  U 109-72-8 BuLi
              SOL  110-54-3 Hexane

            STAGE(3)
              RCT  T 141750-56-3
              SOL  109-99-9 THF

          PRO  CM 141750-57-4

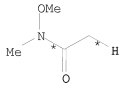
RX(40)    RCT  CM 141750-57-4

            STAGE(1)
              RGT  BL 1191-15-7 AlH(Bu-i)2
              SOL  109-99-9 THF, 110-54-3 Hexane

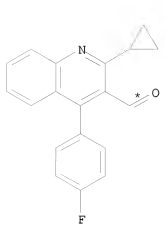
            STAGE(2)
              RGT  CO 7757-82-6 Na2SO4
              SOL  7732-18-5 Water

          PRO  CN 141750-61-0
          NTE  stereoselective

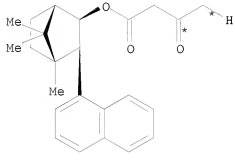

RX(102) OF 163 COMPOSED OF RX(46), RX(45), RX(38), RX(40)
RX(102)   CV  +  S  +  BF  ===>  CN
```



CV

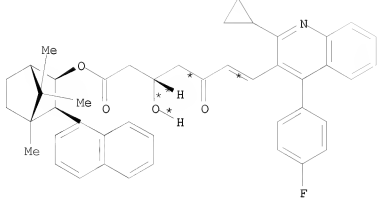


S



BF

4
STEPS



CN
YIELD 56%

```
RX(46)    RCT  CV 78191-00-1

            STAGE(1)
              RGT  CW 4111-54-0 LiN(Pr-i)2
              SOL  110-54-3 Hexane, 109-99-9 THF

            STAGE(2)
              RCT  S 121660-37-5
              SOL  109-99-9 THF

            STAGE(3)
              RGT  I 7732-18-5 Water

          PRO  CS 155849-96-0
          NTE  in-situ generated reagent

RX(45)    RCT  CS 155849-96-0

            STAGE(1)
              RGT  CT 124-63-0 MeSO2Cl, CU 121-44-8 Et3N
              SOL  75-09-2 CH2Cl2

            STAGE(2)
              RGT  CU 121-44-8 Et3N

            STAGE(3)
              RGT  AW 144-55-8 NaHCO3
              SOL  7732-18-5 Water

          PRO  T 141750-56-3
          NTE  alternative prepn. shown, stereoselective

RX(38)    RCT  BF 86835-21-4

            STAGE(1)
              RGT  AB 7646-69-7 NaH
              SOL  109-99-9 THF

            STAGE(2)
              RGT  U 109-72-8 BuLi
              SOL  110-54-3 Hexane

            STAGE(3)
              RCT  T 141750-56-3
              SOL  109-99-9 THF

          PRO  CM 141750-57-4

RX(40)    RCT  CM 141750-57-4

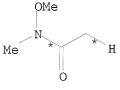
            STAGE(1)
              RGT  BL 1191-15-7 AlH(Bu-i)2
              SOL  109-99-9 THF, 110-54-3 Hexane

            STAGE(2)
              RGT  CO 7757-82-6 Na2SO4
```

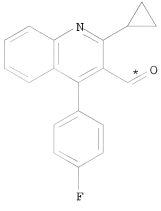
SOL 7732-18-5 Water

PRO CN 141750-61-0
NTE stereoselective

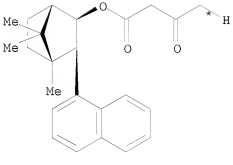
RX(148) OF 163 COMPOSED OF RX(46), RX(45), RX(38)
RX(148) CV + S + BF ===> CM



CV

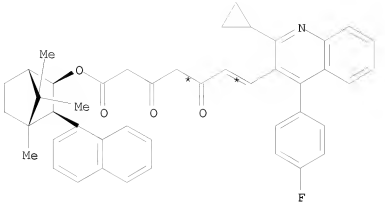


S



3
STEPS

BF



CM
YIELD 48%

RX(46) RCT CV 78191-00-1

STAGE(1)
RGT CW 4111-54-0 LiN(Pr-i)2
SOL 110-54-3 Hexane, 109-99-9 THF

STAGE(2)
RCT S 121660-37-5
SOL 109-99-9 THF

STAGE(3)
RGT I 7732-18-5 Water

PRO CS 155849-96-0
NTE in-situ generated reagent

RX(45) RCT CS 155849-96-0

STAGE(1)
RGT CT 124-63-0 MeSO2Cl, CU 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT CU 121-44-8 Et3N

STAGE(3)
RGT AW 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO T 141750-56-3
NTE alternative prepn. shown, stereoselective

RX(38) RCT BF 86835-21-4

STAGE(1)
RGT AB 7646-69-7 NaH

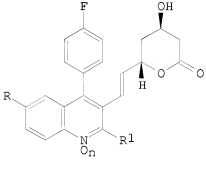
SOL 109-99-9 THF

STAGE(2)
RGT U 109-72-8 BuLi
SOL 110-54-3 Hexane

STAGE(3)
RCT T 141750-56-3
SOL 109-99-9 THF

PRO CM 141750-57-4

L3 ANSWER 11 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 114:61895 CASREACT
TITLE: Inhibitors of cholesterol biosynthesis. 4. trans-6-[2-(Substituted-quinolinyl)ethenyl/ethyl]tetrahydro-4-hydroxy-2H-pyran-2-ones, a novel series of HMG-CoA reductase inhibitors
AUTHOR(S): Sliskovic, D. R.; Picard, J. A.; Roark, W. H.; Roth, B. D.; Ferguson, E.; Krause, B. R.; Newton, R. S.; Sekerke, C.; Shaw, M. K.
CORPORATE SOURCE: Parke-Davis Pharm. Res. Div., Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SOURCE: Journal of Medicinal Chemistry (1991), 34(1), 367-73
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

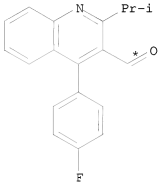


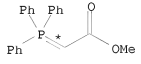
I

AB A series of substituted quinoline mevalonolactones I (n = 0, R = H, Cl, F, OMe, R1 = CHMe2; R = Cl, R1 = Me; R = H, R1 = NMe2; n = 1, R = F, R1 = NMe2) were prepared and evaluated for their ability to inhibit the enzyme HMG-CoA reductase both in vitro and in vivo cholesterol biosynthesis. Since previous studies suggested that the 4-(4-fluorophenyl) and 2-(1-methylethyl) substituents afforded optimum potency, attention was focused on variations at position 6 of the quinoline ring. Biol.

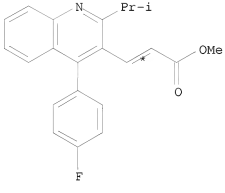
evaluation of a small number of analogs bearing a variety of 6-substituents showed that modification at this position had little effect on potency. I (n = 0, R = Cl, OMe, R1 = CHMe2; n = 1, R = F, R1 = CHMe2) showed comparable potency to compactin and mevinolin in both the in vitro and in vivo assays.

RX(3) OF 68 ...E + I ===> J...





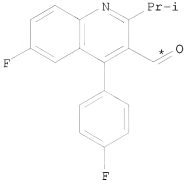
E I (3)



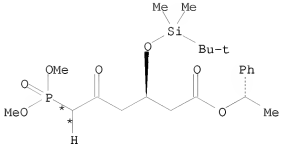
J
YIELD 74%

RX(3) RCT E 121659-66-3, I 2605-67-6
PRO J 130954-90-4
SOL 75-09-2 CH2Cl2

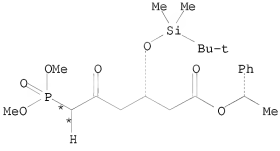
RX(18) OF 68 2 BC + BD + BE ===> Z + AA...


N
Pr-i
F
O
F

2 BC

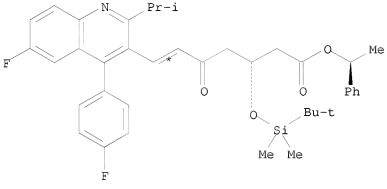

Me Me
Si
Bu-t
O
OMe
O
O
Ph
O
P
MeO
O
O
Me
H

BD

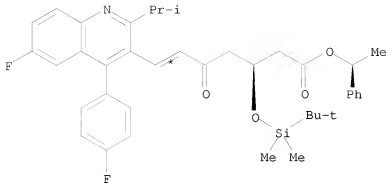

Me Me
Si
Bu-t
O
OMe
O
O
Ph
O
P
MeO
O
O
Me
H

BE

(18)


N
Pr-i
F
O
O
O
Me
Ph
O
Bu-t
Si
Me Me
F

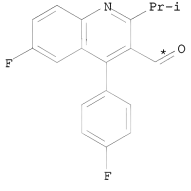
Z



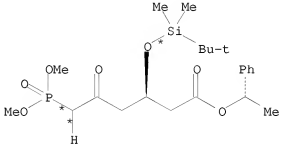
AA

RX(18) RCT BC 130955-11-2, BD 130954-95-9, BE 96555-57-6
RGT BF 7447-41-8 LiCl, BG 6674-22-2 DBU
PRO Z 130954-96-0, AA 130984-01-9
SOL 75-09-2 CH2Cl2

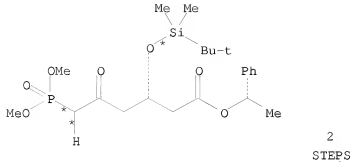
RX(33) OF 68 COMPOSED OF RX(18), RX(8)
RX(33) 2 BC + BD + BE ===> AB + AC



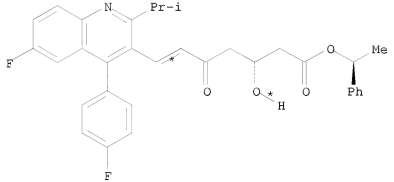
2 BC



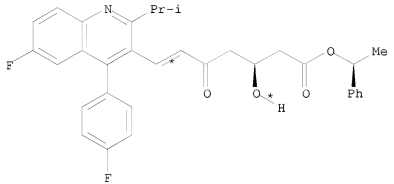
BD



BE



AB



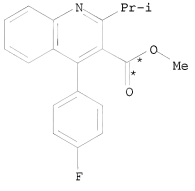
AC

RX(18) RCT BC 130955-11-2, BD 130954-95-9, BE 96555-57-6
RGT BF 7447-41-8 LiCl, BG 6674-22-2 DBU
PRO Z 130954-96-0, AA 130984-01-9

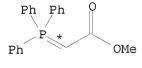
SOL 75-09-2 CH2Cl2

RX(8) RCT Z 130954-96-0, AA 130984-01-9
RGT AD 7664-39-3 HF
PRO AB 130955-12-3, AC 130955-13-4
SOL 75-05-8 MeCN, 7732-18-5 Water
NTE 89% Overall

RX(36) OF 68 COMPOSED OF RX(1), RX(2), RX(3)
RX(36) A + I ===> J

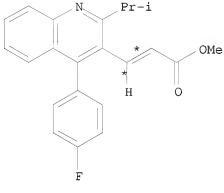


A



I

3
STEPS



J
YIELD 74%

RX(1) RCT A 130954-89-1
RGT C 1191-15-7 AlH(Bu-i)2
PRO B 121659-65-2
SOL 75-09-2 CH2Cl2

RX(2) RCT B 121659-65-2

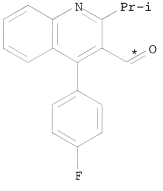
STAGE(1)
RGT F 79-37-8 (COCl)2, G 67-68-5 DMSO
SOL 75-09-2 CH2Cl2

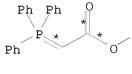
STAGE(2)
RGT H 121-44-8 Et3N

PRO E 121659-66-3

RX(3) RCT E 121659-66-3, I 2605-67-6
PRO J 130954-90-4
SOL 75-09-2 CH2Cl2

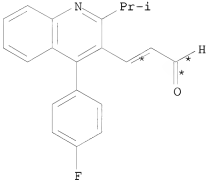
RX(42) OF 68 COMPOSED OF RX(3), RX(4), RX(5)
RX(42) E + I ===> L





3
STEPS

E I



L
YIELD 94%

RX(3) RCT E 121659-66-3, I 2605-67-6
PRO J 130954-90-4

SOL 75-09-2 CH2Cl2

RX(4) RCT J 130954-90-4
RGT C 1191-15-7 AlH(Bu-i)2
PRO K 130954-91-5
SOL 75-09-2 CH2Cl2

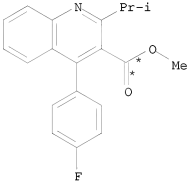
RX(5) RCT K 130954-91-5

STAGE(1)
RGT F 79-37-8 (COCl)2, G 67-68-5 DMSO
SOL 75-09-2 CH2Cl2

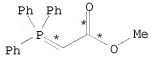
STAGE(2)
RGT H 121-44-8 Et3N

PRO L 121659-68-5

RX(57) OF 68 COMPOSED OF RX(1), RX(2), RX(3), RX(4), RX(5)
RX(57) A + I ===> L

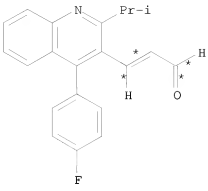


A



I

5
STEPS



L
YIELD 94%

RX(1) RCT A 130954-89-1
RGT C 1191-15-7 AlH(Bu-i)2
PRO B 121659-65-2
SOL 75-09-2 CH2Cl2

RX(2) RCT B 121659-65-2

STAGE(1)
RGT F 79-37-8 (COCl)2, G 67-68-5 DMSO
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT H 121-44-8 Et3N

PRO E 121659-66-3

RX(3) RCT E 121659-66-3, I 2605-67-6
PRO J 130954-90-4
SOL 75-09-2 CH2Cl2

RX(4) RCT J 130954-90-4
RGT C 1191-15-7 AlH(Bu-i)2
PRO K 130954-91-5
SOL 75-09-2 CH2Cl2

RX(5) RCT K 130954-91-5

STAGE(1)
RGT F 79-37-8 (COCl)2, G 67-68-5 DMSO
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT H 121-44-8 Et3N

PRO L 121659-68-5

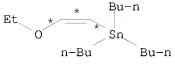
L3 ANSWER 12 OF 12 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 111:134010 CASREACT
TITLE: Quinolinylheptenoic acid derivatives as anticholesteremics, their preparation, and formulations containing them
INVENTOR(S): Fujikawa, Yoshihiro; Suzuki, Mikio; Iwasaki, Hiroshi; Sakashita, Mitsuaki; Kitahara, Masaki
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 304063	A2	19890222	EP 1988-113448	19880818
EP 304063	A3	19901003		
EP 304063	B1	19941130		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 01279866	A	19891110	JP 1988-193606	19880803
JP 2569746	B2	19970108		
CA 1336714	C	19950815	CA 1988-574999	19880817
ES 2067460	T3	19950401	ES 1988-113448	19880818
US 5011930	A	19910430	US 1990-483720	19900223
US 5102888	A	19920407	US 1990-483724	19900223
US 5185328	A	19930209	US 1990-483829	19900223
US 5872130	A	19990216	US 1990-631092	19901219
US 5856336	A	19990105	US 1992-883398	19920515
US 5854259	A	19981229	US 1992-978884	19921119

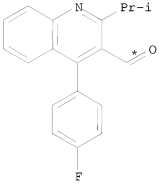
PRIORITY APPLN. INFO.: JP 1987-207224 19870820
JP 1988-15585 19880126
JP 1988-193606 19880803
US 1988-233752 19880819
US 1990-631092 19901219
US 1992-883398 19920515

OTHER SOURCE(S): MARPAT 111:134010
GI For diagram(s), see printed CA Issue.
AB The title compds. I [R1-R4, R6 = H, C1-6 alkyl, C3-6 cycloalkyl, C1-3 alkoxy, etc.; or R1 and R2, R3 and R4 may form CH:CHCH:CH, etc.; Y = CH2, CH2CH2, CH:CH, CH2CH:CH, CH:CHCH2; Z = QCH2WCH2CO2R12, Q1, etc.; Q = C(O), CH(OH), etc.; W = C(O), C(R11)(OH), etc.; R11 = H, C1-6 alkyl; R12 = H, R14; R14 = physiol. hydrolyzable alkyl, M; M = NH4, Na, K, etc.; R5 = H, C1-6 alkyl, C2-3 alkenyl, C3-6 cycloalkyl, etc.], useful as cholesterol biosynthesis inhibitors, were prepared Reduction of Et (E)-7-[4'-(4''-fluorophenyl)-2'-(1'''-methylethyl)quinolin-3'-yl]-5-hydroxy-3-oxohept-6-enoate (preparation given) with NaBH4, followed by saponification in 0.5N NaOH, gave (E)-3,5-dihydroxy-7-[4'-(4''-fluorophenyl)-2'-(1'''-methylethyl)-quinolin-3'-yl]-hept-6-enoic acid Na salt (II). II exhibited an IC50 of 1.0 + 10-8M against cholesterol biosynthesis from acetate in vitro. A capsule formulation containing II 1, lactose 3.5, cellulose 10, Mg stearate 0.5 g is given.

RX(67) OF 137 COMPOSED OF RX(2), RX(3)
RX(67) C + B ===> G

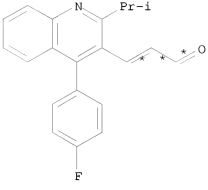


C



B

2
STEPS



G
YIELD 50%

RX(2) RCT C 64724-29-4, B 121659-66-3
       RGT E 109-72-8 BuLi
       PRO D 121659-67-4
       SOL 109-99-9 THF

RX(3) RCT D 121659-67-4
       RGT H 104-15-4 TsOH
       PRO G 121659-68-5
       SOL 109-99-9 THF

=> d his

     (FILE 'HOME' ENTERED AT 11:17:58 ON 30 APR 2008)

     FILE 'REGISTRY' ENTERED AT 11:18:15 ON 30 APR 2008

     FILE 'CASREACT, CHEMINFORMRX, DJSMONLINE, PS' ENTERED AT 11:18:19 ON 30
     APR 2008
L1   STRUCTURE UPLOADED
L2   14 S L1

```
     FILE 'CASREACT' ENTERED AT 11:20:52 ON 30 APR 2008
L3            12 S L1 FULL

=> file reg

=>
Uploading C:\Program Files\Stnexp\Queries\551777.str
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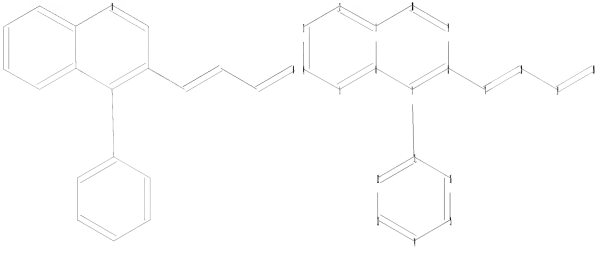
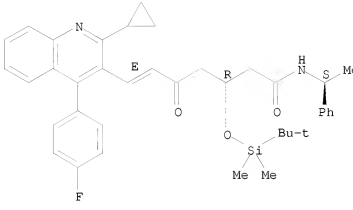


```
chain nodes :
17  18  19  20
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16
chain bonds :
7-11  8-17  17-18  18-19  19-20
ring bonds :
1-2  1-6  1-10  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  11-12  11-16  12-13  13-14
 14-15  15-16
exact/norm bonds :
19-20
exact bonds :
7-11  8-17  17-18  18-19
normalized bonds :
1-2  1-6  1-10  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  11-12  11-16  12-13  13-14
 14-15  15-16


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:CLASS  18:CLASS  19:CLASS
20:CLASS



L4      STRUCTURE UPLOADED

=> s l4 full
```

```
L6            73 SEA SSS FUL L4

=> file ca

=> s l6/p
L7            36 L6/P

=> d ibib abs fhitstr 1-36

L7   ANSWER 1 OF 36  CA  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        148:403055  CA
TITLE:                   A new and efficient synthesis of the HMG-CoA reductase
                         inhibitor pitavastatin. [Erratum to document cited in
                         CA147:300962]
AUTHOR(S):               Acemoglu, Murat; Brodbeck, Andre; Garcia, Angel;
                         Grimler, Dominique; Hassel, Marc; Riss, Bernhard;
                         Schreiber, Robert
CORPORATE SOURCE:        Chemical & Analytical Development, Process Research &
                         Development, Novartis Pharma AG, Basel, CH-4002,
                         Switz.
SOURCE:                  Helvetica Chimica Acta (2007), 90(7), 1447
                         CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER:               Verlag Helvetica Chimica Acta
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   The chemical structure of NK-104 in Scheme 3 was incorrect.  The correct
     structure of NK-104 is given.  On page 1077, 374.4 mL should be changed to
     374.4 g in line 16.  On page 1078, 42.4 mmol should be changed to 44.9
     mmol in line 15.
IT   573690-21-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (improved procedure for preparation of pitavastatin quinolinyl
        dihydroxyheptenoate by asym. ring opening of 3-(silyloxy)glutaric
        anhydride by chiral amines (Erratum))
RN   573690-21-8  CA
CN   6-Heptenamide, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-[[(1,1-
     dimethylethyl)dimethylsilyl]oxy]-5-oxo-N-[(1S)-1-phenylethyl]-, (3R,6E)-
     (CA INDEX NAME)

Absolute stereochemistry.  Rotation (-).
Double bond geometry as shown.
```



L7 ANSWER 2 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 148:302252 CA
TITLE: Carbonyl reductase from Ogataea minuta, gene encoding the same, and process for producing optically active alcohols using the same
INVENTOR(S): Hiraoka, Hirotoshi; Ueda, Makoto; Hara, Mari
PATENT ASSIGNEE(S): Mitsubishi Chemical Corporation, Japan; Nissan Chemical Industries, Ltd.
SOURCE: U.S., 25pp., Cont.-in-part of Appl. No. PCT/JP03/3262. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7335757	B2	20080226	US 2004-943202	20040917
US 20050048633	A1	20050303		
WO 2003078634	A1	20030925	WO 2003-JP3262	20030318

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-75921 A 20020319
WO 2003-JP3262 A2 20030318
OTHER SOURCE(S): CASREACT 148:302252

AB A novel carbonyl reductase derived from Ogataea minuta var. nonfermentans is provided as well as a DNA encoding the enzyme. By reducing ketones with the use of the carbonyl reductase, optically active alcs., in particular, (E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid esters can be produced. The carbonyl reductase according to the present invention is excellent in activity and

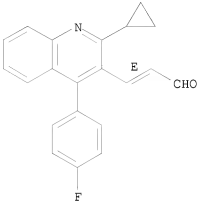
stereoselectivity. Thus, according to the present invention, there is provided a process for producing optically active alcs., which are industrially useful as intermediate materials for drugs, pesticides, etc.

IT 148901-68-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(carbonyl reductase from Ogataea minuta, gene encoding the same, and process for producing optically active alcs. using the same)

RN 148901-68-2 CA

CN 2-Propenal, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 36 CA COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 147:300962 CA

TITLE: A new and efficient synthesis of the HMG-CoA reductase inhibitor pitavastatin

AUTHOR(S): Acemoglu, Murat; Brodbeck, Andre; Garcia, Angel; Grimler, Dominique; Hassel, Marc; Riss, Bernhard; Schreiber, Robert

CORPORATE SOURCE: Chemical & Analytical Development, Process Research & Development, Novartis Pharma AG, Basel, CH-4002, Switz.

SOURCE: Helvetica Chimica Acta (2007), 90(6), 1069-1081
CODEN: HCACAV; ISSN: 0018-019X

PUBLISHER: Verlag Helvetica Chimica Acta

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 147:300962

AB An improved synthetic procedure for the preparation of pitavastatin, calcium 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-(3R,5S,6E)-6-heptenoate, based on asym. ring opening of 3-TBDMSO-glutaric anhydride (1) by chiral amines, is described. Ring opening of 1 in the reaction with (1S)-1-phenylethylamine (R*NH2, 2c) gave the carbamoylbutanoic acid, (3S)-R*NHCOCH2CH(OTBDMS)CH2CO2H (3c), which was converted to Weinreb amide and phosphonylated to give β-oxophosphonate (4S)-R*NHCOCH2CH(OTBDMS)CH2COCH2P(O)(OMe)2 (5) in reaction with

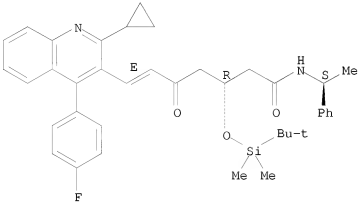
LiCH2P(O)(OMe)2. Use of bulkier amines in the asym. ring opening of 1 did not lead to improvement of enantioselectivity. Compound 5 was reacted with 2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinecarboxaldehyde (8) and after stereoselective reduction of the keto-group hydrolyzed to target compound, pitavastatin and its δ-lactone, NK-104. The approach circumvents various synthetic problems associated with the buildup of the 3,5-dihydroxy-C7 acid side chain of HMG-CoA reductase inhibitors (statins). The use of the C6-amide derivative 5 instead of ester derivs. in the coupling reaction with carboxaldehyde 8 prevents undesired elimination and retro-aldol side reactions. The method provides synthetic statins, such as pitavastatin, in > 99% ee and exceptionally high overall yield.

IT 573690-21-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(improved procedure for preparation of pitavastatin quinolinyl dihydroxyheptenoate by asym. ring opening of 3-(silyloxy)glutaric anhydride by chiral amines)

RN 573690-21-8 CA

CN 6-Heptenamide, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-oxo-N-[(1S)-1-phenylethyl]-, (3R,6E)-(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



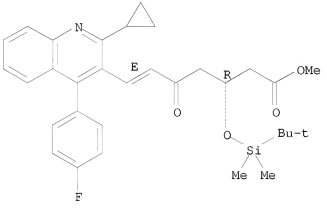
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 146:100564 CA
TITLE: Preparation of Pitavastatin calcium with high optical purity as HMG-CoA reductase inhibitor
INVENTOR(S): Wu, Hao; Hu, Guoping; Du, Xiaoxing; Li, Ge
PATENT ASSIGNEE(S): Shanghai Pharmatech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 14pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1876633	A	20061213	CN 2005-10026641	20050610

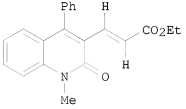
PRIORITY APPLN. INFO.: CN 2005-10026641 20050610
OTHER SOURCE(S): CASREACT 146:100564; MARPAT 146:100564
AB In this invention, Pitavastatin calcium is prepared from 2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-carbaldehyde with (3R)-3-alkylsiloxoxane-5-carbonyl-6-triphenylphosphoric heptenoate via Wittig reaction to form (E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinoline]-5-carbonyl-(3R)-3-alkylsiloxoxane-6-heptenoate, then deprotection of the alkylsilyl group to obtain (E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinoline]-5-carbonyl-(3R)-hydroxy-6-heptenoate, further selective reduction with NaBH4 or KBH4 in the presence of ligand in a mixed solvents of alc. and ether to give (E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinoline]-(3R,5S)-dihydroxy-6-heptenoate, after hydrolysis with a base to obtain Pitavastatin calcium. Pitavastatin calcium is mainly used as HMG-CoA reductase inhibitor (a hypolipidemic drug).
IT 182075-76-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(high optical purity Pitavastatin calcium preparation and application as HMG-CoA reductase inhibitor)
RN 182075-76-9 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-oxo-, methyl ester, (3R,6E)-(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



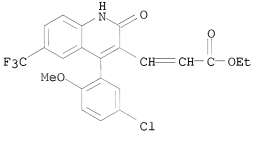
L7 ANSWER 5 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 142:481926 CA
TITLE: Microwave-assisted multistep synthesis of functionalized 4-arylquinolin-2(1H)-ones using palladium-catalyzed cross-coupling chemistry
AUTHOR(S): Glasnov, Toma N.; Stadlbauer, Wolfgang; Kappe, C. Oliver
CORPORATE SOURCE: Institute of Chemistry Organic and Bioorganic Chemistry, Karl-Franzens-University Graz, Graz, A-8010, Austria

SOURCE: Journal of Organic Chemistry (2005), 70(10), 3864-3870
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:481926
GI



I

AB Biol. active 4-aryl-3-alkenyl-substituted quinolin-2(1H)-ones, e.g., I, have been synthesized in a short and concise manner employing readily available 4-hydroxyquinolin-2(1H)-ones as intermediates. Key steps in the synthesis included the derivatization of the quinolin-2(1H)-one cores using palladium-catalyzed Suzuki and Heck reactions, installing the 4-aryl and 3-alkenyl substituents. All synthetic transformations (six steps) required for the synthesis of the desired target quinolin-2(1H)-one were carried out using controlled microwave-assisted organic synthesis.
IT 852203-20-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of aryl(ethoxycarbonylvinyl)quinolinones via microwave-mediated palladium-catalyzed Heck reaction of aryl(bromo)quinolinones with acrylate)
RN 852203-20-4 CA
CN 2-Propenoic acid, 3-[4-(5-chloro-2-methoxyphenyl)-1,2-dihydro-2-oxo-6-(trifluoromethyl)-3-quinolinyl]-, ethyl ester (CA INDEX NAME)

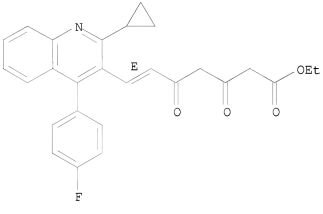


REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 142:481922 CA
TITLE: Asymmetric reduction using biocatalytic reactions
AUTHOR(S): Okano, Kazuya; Ueda, Makoto
CORPORATE SOURCE: API Business Division, API Corporation, Japan
SOURCE: Speciality Chemicals Magazine (2004), 24(11), 40-41

CODEN: SPCHEY; ISSN: 0262-2262
PUBLISHER: DMG World Media (uk) Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An enzyme expressed in a recombinant microorganism exhibited activity for the preparation of Pitavastatin Et ester by diastereoselective reduction of the 3-keto-5-hydroxy and double enantioselective reduction of the 3,5-diketo ester precursors.
IT 166803-31-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(double enantioselective enzymic reduction; asym. reduction using biocatalytic reactions)
RN 166803-31-2 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, ethyl ester, (6E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

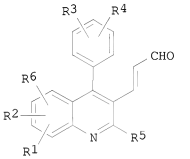
L7 ANSWER 7 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 141:366139 CA
TITLE: Process for preparation of quinoline derivatives
INVENTOR(S): Fukumoto, Takashi; Nagashima, Kensuke
PATENT ASSIGNEE(S): Kuraray Co., Ltd., Japan; Nissan Chemical Industries, Ltd.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089907	A1	20041021	WO 2004-JP2464	20040301
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

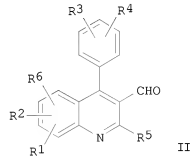
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

AU 2004228485	A1	20041021	AU 2004-228485		20040301
CA 2521238	A1	20041021	CA 2004-2521238		20040301
EP 1614682	A1	20060111	EP 2004-716036		20040301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK					
CN 1768039	A	20060503	CN 2004-80008724		20040301
US 20060276653	A1	20061207	US 2005-551777		20051003
IN 2005CN02856	A	20070525	IN 2005-CN2856		20051103
PRIORITY APPLN. INFO.:			JP 2003-102134	A	20030404
			WO 2004-JP2464	W	20040301

OTHER SOURCE(S): MARPAT 141:366139
GI



I



II

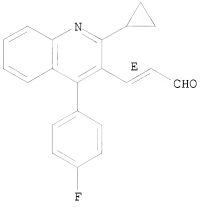
AB This invention pertains to a method for producing quinoline derivs. represented by the general formula I [wherein R1-R6 = independently H, halo, (un)substituted OH, alkyl, aryl, aralkyl, alkoxy, or aryloxy], which comprises reacting a quinolinecarbaldehyde II with an imine compound MeCH=NR7 [where R7 = (un)substituted alkyl] and subsequently hydrolyzing the reaction product. For example, tert-butylamine was reacted with acetaldehyde to give MeCH=N-Bu-t (81.0%). The imine was reacted with 4-(4-fluorophenyl)-2-cyclopropylquinoline-3-carbaldehyde in THF in the presence of NaH to afford (E)-3-[4-(4-fluorophenyl)-2-cyclopropylquinolin-3-yl]propenaldehyde (68.0%). This invention provides a short process to prepare quinoline derivs. with industrial advantages.

IT 148901-68-2P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of quinoline derivs.)

RN 148901-68-2 CA

CN 2-Propenal, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.

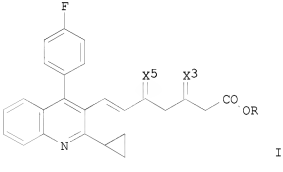


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 140:41958 CA
TITLE: Process for the manufacture of organic compounds
INVENTOR(S): Storz, Thomas
PATENT ASSIGNEE(S): Novartis AG, USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030233001	A1	20031218	US 2003-428257	20030502
US 6909003	B2	20050621		
PRIORITY APPLN. INFO.:			GB 2002-10234 A	20020503

OTHER SOURCE(S): MARPAT 140:41958
GI



I

AB This invention relates to a process for the manufacture of analogs, (3R,5R)-R1(CH2)2CH(OH)CH2CH(OH)CH2CO2H and (3R,5S,6E)-

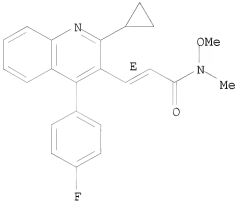
R1CH:CHCH(OH)CH2CH(OH)CH2CO2H [R1 = cyclic statin analog residue], of known HMG-CoA reductase inhibiting statins via an enantioselective reduction using a ruthenium catalyst. Thus, pitavastatin hemicalcium salt (3R,5S,6E)-I (R = 1/2Ca2+, X3 = X5 = β-OH-α-H) was prepared via enantioselective reduction of 3,5-dioxo-ester (6E)-I (R = Et, X3 = X5 = O) catalyzed by (1R,2R)-N-p-toluenesulfonyl-1,2-diphenylethylenediamine-RuII-p-cymene complex in DMF followed by treatment with Et3N to give 3,5-diol-ester (3R,5S,6E)-I (R = Et, X3 = X5 = β-OH-α-H) which was subsequently converted to the target hemicalcium salt.

IT 141750-56-3P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for asym. synthesis of analogs of statins via enantioselective reduction using a ruthenium catalyst)

RN 141750-56-3 CA

CN 2-Propenamide, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-N-methoxy-N-methyl-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 139:337984 CA
TITLE: Preparation of rosuvastatin and related HMG-CoA reductase inhibitors via a common chiral intermediate
INVENTOR(S): Lim, Kwang-Min
PATENT ASSIGNEE(S): CLS Laboratories, Inc., S. Korea
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

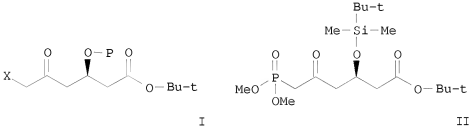
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003087112	A1	20031023	WO 2003-KR707	20030409

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

KR 2003080620	A	20031017	KR 2002-19340		20020409
AU 2003219592	A1	20031027	AU 2003-219592		20030409
PRIORITY APPLN. INFO.:			KR 2002-19340	A	20020409
			WO 2003-KR707	W	20030409

OTHER SOURCE(S): CASREACT 139:337984; MARPAT 139:337984
GI



I II

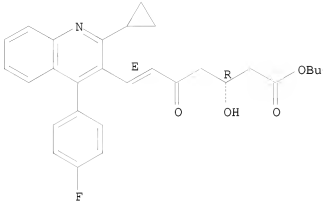
AB A process for the preparation of rosuvastatin and related HMG-CoA reductase inhibitors via the common chiral intermediate I [X = P(=O)R12, S(O)R1; R1 = H, alkyl, aryl; P = OH protecting group, e.g., t-butyldimethylsilyl] was disclosed. For example, condensation of Et tert-Bu (3R)-3-hydroxyglutaric acid, e.g., prepared from diethyl-3-hydroxyglutaric acid in 3-steps, and the sodium salt of di-Me methylphosphonate afforded claimed chiral phosphonate II in 77% yield and 99.1% chiral purity. Of note is the enantioselective esterase mediated hydroylsis of diethyl-3-hydroxyglutaric acid in 99.5% chiral purity. The preparation of the sodium salt of rosuvastatin using chiral phosphonate II was also provided. The present invention does not have the problem of removing reaction byproducts and the disposal of waste associated with current methodologies.

IT 615556-97-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of rosuvastatin and related HMG-CoA reductase inhibitors via a common chiral intermediate)

RN 615556-97-3 CA

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, 1,1-dimethylethyl ester, (3R,6E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



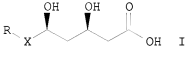
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 139:214343 CA
TITLE: Process for the manufacture of HMG-CoA reductase inhibitory mevalonic acid derivatives
INVENTOR(S): Sedelmeier, Gottfried; Mathes, Christian
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070717	A1	20030828	WO 2003-EP1738	20030220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
CA 2473075	A1	20030823	CA 2003-2473075	20030220
AU 2003218994	A1	20030909	AU 2003-218994	20030220
AU 2003218994	B2	20070809		
EP 1478640	A1	20041124	EP 2003-714750	20030220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007801	A	20041221	BR 2003-7801	20030220
CN 1636004	A	20050706	CN 2003-804288	20030220
JP 2005520818	T	20050714	JP 2003-569624	20030220
NZ 534394	A	20061027	NZ 2003-534394	20030220
ZA 2004005436	A	20050617	ZA 2004-5436	20040708
US 20050159480	A1	20050721	US 2004-504655	20040813
US 7208623	B2	20070424		

	IN 2004CN01834	A	20070921	IN 2004-CN1834		20040817
	MX 2004PA08110	A	20041126	MX 2004-PA8110		20040820
	NO 2004003919	A	20040920	NO 2004-3919		20040920
	US 2007015570	A1	20070705	US 2007-684134		20070309
PRIORITY APPLN. INFO.:				GB 2002-4129	A	20020221
				WO 2003-EP1738	W	20030220
				US 2004-504655	A3	20040813

OTHER SOURCE(S): MARPAT 139:214343
GI

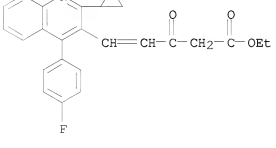


AB Mevalonic acid derivs. I [R = cyclic residue; X = CH2CH2, CH:CH] are prepared by treating R1R2R3P:CHCOCH2CO2R4 [R1-R3 = (un)substituted Ph; R4 = aliphatic, cycloaliph., aromatic] with RCHO, reducing the resulting RCH:CHCOCH2CO2R4 in presence of a chiral metal BINAP or TsDPEN catalyst, treating the resulting alc. with an ester enolate, reducing the second oxo group, and hydrolyzing the ester group. Thus, ClCH2COCH2CO2Et was treated with PPh3 to give Ph3P:CHCOCH2CO2Et which was treated with 2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-carboxaldehyde to give (E)-5-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3-oxopent-4-enoic acid Et ester. This ester was reduced with Ru[(1R,2R)-p-TsNCHPhCHPhNH](η-p-cymene) and treated with Me3COAc to give (E)-(S)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-5-hydroxy-3-oxohept-4-enoic acid tert.-Bu ester which was reduced with MeOBEt2 and hydrolyzed to give (E)-(3R,5S)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxyhept-4-enoic acid calcium salt.

IT 586966-50-9P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for the manufacture of HMG-CoA reductase inhibitory mevalonic acid derivs.)

RN 586966-50-9 CA

CN 4-Pentenoic acid, 5-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-oxo-, ethyl ester (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 139:178816 CA
TITLE: Optically active hydroxyketo esters manufacture with microorganism
INVENTOR(S): Asano, Yasuhisa; Suzuki, Kenji; Matsumoto, Hiroo
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003235595	A	20030826	JP 2002-38670	20020215
JP 3932926	B2	20070620		
PRIORITY APPLN. INFO.:			JP 2002-38670	20020215

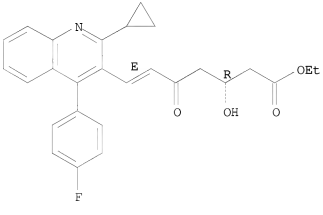
OTHER SOURCE(S): MARPAT 139:178816

AB The title optically active hydroxyketo esters (I) are manufactured by asym. reduction with microorganism such as Saccharomyces cerevisiae. I, especially (3R,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3-hydroxy-5-oxy-6-heptanoic acid Et ester, are useful intermediates for manufacture of HMG-CoA reductase inhibitors which are useful for preparing hypocholesteremics.

IT 444732-68-7P
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(optically active hydroxyketo esters manufacture with microorganism by asym. reduction)

RN 444732-68-7 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, ethyl ester, (3R,6E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



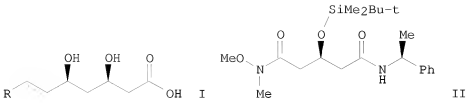
L7 ANSWER 12 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 139:149536 CA
TITLE: Preparation of an asymmetric β,δ-dihydroxycarboxylic acid side chain used for the

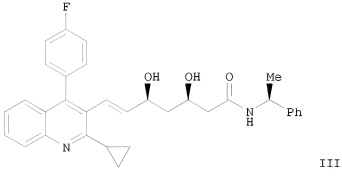
manufacture of a HMG-CoA reductase inhibitors
INVENTOR(S): Acemoglu, Murat; Riss, Bernhard
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003064392	A1	20030807	WO 2003-EP954	20030130
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
CA 2472776	A1	20030807	CA 2003-2472776	20030130
EP 1472228	A1	20041103	EP 2003-734716	20030130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007303	A	20050111	BR 2003-7303	20030130
CN 1622937	A	20050601	CN 2003-802740	20030130
JP 2005520814	T	20050714	JP 2003-564015	20030130
NZ 534232	A	20060331	NZ 2003-534232	20030130
RU 2299196	C2	20070520	RU 2004-126442	20030130
ZA 2004005322	A	20050617	ZA 2004-5322	20040705
US 20050070605	A1	20050331	US 2004-502177	20040721
IN 2004CN01647	A	20060512	IN 2004-CN1647	20040726
MX 2004PA07396	A	20041011	MX 2004-PA7396	20040730
NO 2004003611	A	20040830	NO 2004-3611	20040830

PRIORITY APPLN. INFO.: US 2002-353787P P 20020131
WO 2003-EP954 W 20030130

OTHER SOURCE(S): MARPAT 139:149536
GI





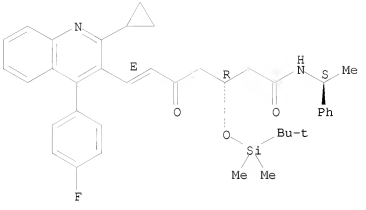
AB A process for the stereoselective preparation of a β,δ-dihydroxycarboxylic acid I [R = cyclic residue] is disclosed. For instance, glutaric acid diamide analog II (preparation given) is reacted with methanephosphonic acid di-Et ester (THF, n-BuLi, -78°) and the resulting phosphonate condensed with [2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]carboxaldehyde (i-PrOH, Cs2CO3) to give the corresponding E-olefin. This intermediate is deprotected and reduced (THF, NaBH4, Me2BOMe, -78°, 30 min) to give III. Addnl. examples demonstrate the conversion of III (optionally via the intermediacy of a 2H-pyran intermediate) to pitavastatin (calcium salt).

IT 573690-21-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of an asym. β,δ-dihydroxycarboxylic acid side chain used for manufacture of a HMG-CoA reductase inhibitors)

RN 573690-21-8 CA

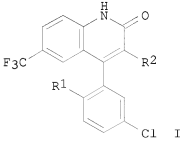
CN 6-Heptenamide, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-oxo-N-[(1S)-1-phenylethyl]-, (3R,6E)-(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 139:133450 CA
TITLE: 4-Aryl-3-(hydroxyalkyl)quinolin-2-ones: Novel Maxi-K Channel Opening Relaxants of Corporal Smooth Muscle Targeted for Erectile Dysfunction
AUTHOR(S): Hewawasam, Piyasena; Fan, Wenhong; Ding, Min; Flint, Kim; Cook, Deborah; Goggins, Gregory D.; Myers, Robert A.; Gribkoff, Valentin K.; Boissard, Christopher G.; Dworetzky, Steven I.; Starrett, John E., Jr.; Lodge, Nicholas J.
CORPORATE SOURCE: Departments of Chemistry and Neuroscience/Genitourinary Drug Discovery, Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT, 06492, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(14), 2819-2822
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:133450
GI



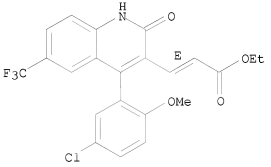
AB Novel 4-aryl-3-(hydroxyalkyl)quinoline-2-ones I [R1 = HO, MeO; R2 = HO(CH2)n, n = 1 - 3; R2 = (E)-HOCH2CH:CH] were prepared and evaluated as openers of the cloned maxi-K channel hSlo expressed in Xenopus laevis oocytes by utilizing electrophysiol. methods. The effect of these maxi-K openers on corporal smooth muscle was studied in vitro using isolated rabbit corpus cavernosum. A potent maxi-K opener was identified as an effective relaxant of rabbit corporal smooth muscle and shown to be active in an in vivo animal model of male erectile function.

IT 275375-54-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl(hydroxyalkyl)quinolinones as maxi-K channel opening relaxants of corporal smooth muscle targeted for erectile dysfunction)

RN 275375-54-7 CA

CN 2-Propenoic acid, 3-[4-(5-chloro-2-methoxyphenyl)-1,2-dihydro-2-oxo-6-(trifluoromethyl)-3-quinolinyl]-, ethyl ester, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 36 CA COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 136:112193 CA

TITLE: Synthesis and biological evaluations of quinoline-based HMG-CoA reductase inhibitors

AUTHOR(S): Suzuki, M.; Iwasaki, H.; Fujikawa, Y.; Kitahara, M.; Sakashita, M.; Sakoda, R.

CORPORATE SOURCE: Central Research Laboratories, Nissan Chemical Industries, Ltd., Funabashi, Chiba, 274-8507, Japan

SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(10), 2727-2743
CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:112193

AB A series of quinoline-based 3,5-dihydroxyheptenoic acid derivs. were synthesized from quinolinecarboxylic acid esters by homologation, aldol condensation with Et acetoacetate dianion, and reduction of 3-hydroxyketone to evaluate their ability to inhibit the enzyme HMG-CoA reductase in vitro. In agreement with previous literature, a strict structural requirement exists on the external ring, and 4-fluorophenyl is the most active in this

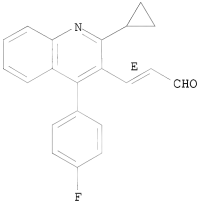
system. For the central ring, substitution on positions 6, 7, and 8 of the central quinoline nucleus moderately affected the potency, whereas the alkyl side chain on the 2-position had a more pronounced influence on activity. Among the derivs., NK-104 (pitavastatin calcium), which has a cyclopropyl group as the alkyl side chain, showed the greatest potency. We found that further modulation and improvement in potency at inhibiting HMG-CoA reductase was obtained by having the optimal substituents flanking the desmethylmevalonic acid portion, i.e., 4-fluorophenyl and cyclopropyl, instead of the usual iso-Pr group.

IT 148901-68-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. evaluations of quinoline-based HMG-CoA reductase inhibitors)

RN 148901-68-2 CA

CN 2-Propenal, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 36 CA COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 135:180711 CA

TITLE: Processes for preparing quinoline derivatives and intermediates thereof

INVENTOR(S): Tatsuta, Kuniaki; Kikuyama, Shigeki; Tamai, Yoshin

PATENT ASSIGNEE(S): Kuraray Co., Ltd., Japan; Nissan Chemical Industries, Ltd.

SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060800	A1	20010823	WO 2001-JP1184	20010219

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

JP 2001316368	A	20011113	JP 2001-37097		20010214
JP 2001316369	A	20011113	JP 2001-37106		20010214
CA 2400977	A1	20010823	CA 2001-2400977		20010219
AU 2001032342	A	20010827	AU 2001-32342		20010219
EP 1262476	A1	20021204	EP 2001-904553		20010219
EP 1262476	B1	20070110			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

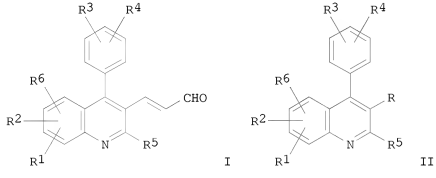
US 20030125355	A1	20030703	US 2002-204312		20021121
US 6855824	B2	20050215			

PRIORITY APPLN. INFO.:

JP 2000-42594	A	20000221
JP 2000-42595	A	20000221
WO 2001-JP1184	W	20010219

OTHER SOURCE(S): CASREACT 135:180711; MARPAT 135:180711

GI



AB A process for preparing quinoline derivs. [I; R1-R6 = H, halo, CF3, CF3O, (un)protected OH, (un)substituted alkyl, cycloalkyl, aryl, aralkyl, alkoxy, or aryloxy] comprises Wittig condensation or Horner-Emmons reaction of a quinolinecarbaldehyde (II; R = CHO; R1-R5) with one member selected from among compds. (R9)3P+CH2CH(OR7)OR8.X- [R7, R8 = H, (un)substituted alkyl, acyl, or aralkyl, or R7 and R8 are joined together to form an alkylene, arylene, or aralkylene; R9 = (un)substituted aralkyl or aryl; X = halo], (R9O)2P(O)CH2CH(OR7)OR8 (R7-R9 = same as above), and (R9O)2P(O)CH:CHNR10R11 [R9 = same as above; R10, R11 = H, (un)substituted alkyl, cycloalkyl, aryl, or aralkyl] in the presence of a base and hydrolyzing the obtained compound The quinolinecarbaldehyde II (R = CHO) are prepared by reduction of quinolinecarboxylic acid esters II [R = CO2R12; R1-R6 = same as above; R12 = (un)substituted alkyl, cycloalkyl, aryl, or aralkyl] with aluminum hydride complex in the presence of a secondary amine. The compound I, e.g. (E)-3-(4-(4-fluorophenyl)-2-cyclopropylquinolin-3-yl)propenaldehyde (III), is useful as an intermediate for quinoline-series mevalonolactone derivative which is known as a HMG-CoA reductase inhibitor in cholesterol biosynthesis. This process is

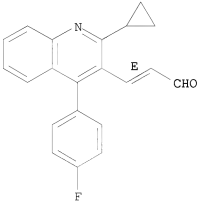
efficient and industrially advantageous since it give I in shorter steps using industrially readily available and easily handled chems. Thus, 4.18 g morpholine was added dropurse slowly to 0.569 g LiAlH4 in 10 mL THF to give the reaction solution which was cooled to 0°, treated dropurse with a solution of 3.21 g Me 4-(4-fluorophenyl)-2-cyclopropylquinoline-3-carboxylate in 9.63 g THF at 0°, and the resulting mixture was stirred at 10-20° for 2 h and treated with 15% aqueous H2SO4 at ≤10° to give, after workup and silica gel chromatog., 77% 4-(4-fluorophenyl)-2-cyclopropylquinoline-3-carbaldehyde (IV). A pentane solution of potassium tert-butoxide (1.51 mL, 2.40 mL) was added dropurse at 20-30° over a period of 2 min to a solution of 1.55 g (1,3-dioxolan-2-ylmethyl)triphenylphosphonium bromide in 10.0 mL anhydrous DMSO, stirred at room temperature for 15 min, treated with a solution of 1.00 g IV in 5 mL anhydrous DMSO at 20-30° over a period of 5 min, and stirred at the same temperature for 90 min. The reaction mixture was treated with 10 mL water followed by separating the organic layer and extracting the water layer with 20 mL hexane twice, and the combined organic layers were washed with water, dried over anhydrous Na2SO4, and concentrated in vacuo. The concentrate residue was dissolved in 20 mL THF, treated with 2 M aqueous HCl, and stirred at room temperature for 30 min to give, after workup and silica gel chromatog., 90.9% III.

IT 148901-68-2P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenylquinolinylpropenal derivs. by aluminum hydride reduction of quinolinecarboxylate esters to quinolinecarbaldehyde derivs. followed by Wittig or Horner-Emmons condensation)

RN 148901-68-2 CA

CN 2-Propenal, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



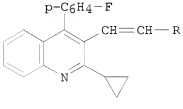
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 135:122410 CA
TITLE: Preparation of quinolylpropenal derivative from quinolylacrylonitrile derivative
INVENTOR(S): Harada, Katsumasa; Nishino, Shigeyoshi; Shima, Hideyoshi; Harada, Takashi; Okada, Shoko
PATENT ASSIGNEE(S): Ube Industries, Ltd., Japan; Nissan Chemical Industries, Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001199964	A	20010724	JP 2000-14849	20000124
CA 2398138	A1	20010726	CA 2001-2398138	20010124
WO 2001053265	A1	20010726	WO 2001-JP452	20010124
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, SE, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001027100	A	20010731	AU 2001-27100	20010124
EP 1251124	A1	20021023	EP 2001-901538	20010124
EP 1251124	B1	20070704		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 366239	T	20070715	AT 2001-901538	20010124
US 20030114680	A1	20030619	US 2002-181820	20021120
US 6630591	B2	20031007		

PRIORITY APPLN. INFO.:
JP 2000-14848 A 20000124
JP 2000-14849 A 20000124
WO 2001-JP452 W 20010124

OTHER SOURCE(S): CASREACT 135:122410
GI



I

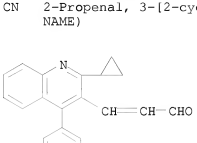
AB Quinolylpropenal derivative I (R = CHO), useful as an intermediate for anticholesteremic agents, is prepared by reduction of quinolylacrylonitrile derivative I (R = cyano) in the presence of Raney Ni, HCO2H amine salt, and

organic acid. Thus, I (R = cyano) was treated with NDHT 90 (Raney Ni), HCO2NH4, and AcOH at 60° for 4 h to give 82% I (R = CHO).

IT 121660-63-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of quinolylpropenal derivative as intermediate for anticholesteremic agents)

RN 121660-63-7 CA

CN 2-Propenal, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]- (CA INDEX NAME)



L7 ANSWER 17 OF 36 CA COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 135:122409 CA

TITLE: Preparation of quinolylacrylonitrile derivative from quinolinecarboxaldehyde derivative

INVENTOR(S): Harada, Katsumasa; Nishino, Shigeyoshi; Okada, Naoko; Shima, Hideyoshi; Harada, Takashi

PATENT ASSIGNEE(S): Ube Industries, Ltd., Japan; Nissan Chemical Industries, Ltd.

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

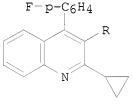
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001199962	A	20010724	JP 2000-14864	20000124
CA 2398113	A1	20010726	CA 2001-2398113	20010124
WO 2001053264	A1	20010726	WO 2001-JP451	20010124
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001027099	A	20010731	AU 2001-27099	20010124
AU 777959	B2	20041104		
EP 1251123	A1	20021023	EP 2001-901537	20010124

EP 1251123	B1	20040721			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
HU 2002004145	A2	20030328	HU 2002-4145		20010124
HU 2002004145	A3	20050530			
NZ 520415	A	20030926	NZ 2001-520415		20010124
AT 271545	T	20040815	AT 2001-901537		20010124
PT 1251123	T	20041130	PT 2001-901537		20010124
ES 2220705	T3	20041216	ES 2001-901537		20010124
RU 2260000	C2	20050910	RU 2002-122754		20010124
ZA 2002005849	A	20031022	ZA 2002-5849		20020722
NO 2002003505	A	20020905	NO 2002-3505		20020723
NO 323397	B1	20070423			
MX 2002PA07182	A	20031125	MX 2002-PA7182		20020723
US 20030013885	A1	20030116	US 2002-181973		20020724
US 6541636	B2	20030401			
PRIORITY APPLN. INFO.:			JP 2000-14864	A	20000124
			WO 2001-JP451	W	20010124

OTHER SOURCE(S): CASREACT 135:122409

GI



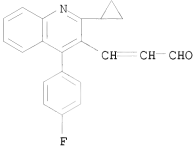
I

AB Quinolylacrylonitrile derivative I (R = trans-CH:CHCN), useful as an intermediate for quinolylpropenal derivative and HMG-CoA reductase inhibitors, is prepared by treatment of quinolinecarboxaldehyde derivative I (R = CHO) with MeCN in the presence of base, then treatment of the resulting mixture of I (R = HOCHCH2CN) and I (R = trans-CH:CHCN) with dehydration agent. Thus, I (R = CHO) was treated with MeCN and NaH at room temperature for 2 h and treated with HCO2Et at -10° for 4 h to give 85% I (R = trans-CH:CHCN).

IT 121660-63-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(intermediate for; preparation of quinolylacrylonitrile derivative from quinolinecarboxaldehyde derivative)

RN 121660-63-7 CA

CN 2-Propenal, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]- (CA INDEX NAME)

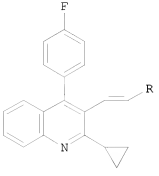


L7 ANSWER 18 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 135:92551 CA
TITLE: Method for preparation of quinolylpropenal by reduction of quinolylacrylonitrile
INVENTOR(S): Harada, Katsumasa; Nishino, Shigeyoshi; Shima, Hideyoshi; Harada, Takashi; Okada, Naoko
PATENT ASSIGNEE(S): Ube Industries, Ltd., Japan; Nissan Chemical Industries, Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001199963	A	20010724	JP 2000-14848	20000124
CA 2398138	A1	20010726	CA 2001-2398138	20010124
WO 2001053265	A1	20010726	WO 2001-JP452	20010124
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, SE, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001027100	A	20010731	AU 2001-27100	20010124
EP 1251124	A1	20021023	EP 2001-901538	20010124
EP 1251124	B1	20070704		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 366239	T	20070715	AT 2001-901538	20010124
US 20030114680	A1	20030619	US 2002-181820	20021120
US 6630591	B2	20031007		

PRIORITY APPLN. INFO.: JP 2000-14848 A 20000124
JP 2000-14849 A 20000124
WO 2001-JP452 W 20010124

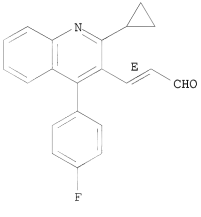
OTHER SOURCE(S): CASREACT 135:92551
GI



I

AB The title compound (I; R = CHO) is prepared by reduction of quinolylacrylonitrile
I (R = cyano) by Raney nickel and formic acid in the presence of 0.25-1 volume-times as much water as formic acid. This process is simple and industrially advantageous and gives in high yield I (R = cyano) which is useful as an intermediate for cholesterol-lowering agents (HMG-CoA reductase inhibitors). Thus, 314 mg I (R = CHO), 2.25 mL formic acid, 0.75 mL H2O, 620 mg Raney nickel (NDHT-90, 50 weight% Ni, Kawaken Fine Chems. Inc., Japan) were stirred at 80° for 1.5 h to give 91% I (R = CHO).
IT 148901-68-2P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of quinolylpropenal derivative by reduction of quinolylacrylonitrile
derivative with Raney nickel and formic acid in presence of water)
RN 148901-68-2 CA
CN 2-Propenal, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-, (2E)- (CA INDEX NAME)

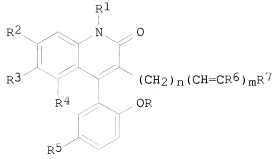
Double bond geometry as shown.



L7 ANSWER 19 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 133:43452 CA
TITLE: Preparation of 3-substituted-4-arylquinolin-2-one derivatives as calcium-activated potassium (BK) channel openers
INVENTOR(S): Hewawasam, Piyasena; Starrett, John E., Jr.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000034244	A1	20000615	WO 1999-US28428		19991201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6184231	B1	20010206	US 1999-452523		19991201
BR 9915744	A	20010821	BR 1999-15744		19991201
EP 1133474	A1	20010919	EP 1999-960636		19991201
EP 1133474	B1	20070221			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY					
TR 200101339	T2	20020221	TR 2001-1339		19991201
JP 2002531549	T	20020924	JP 2000-586692		19991201
HU 2002001613	A2	20020928	HU 2002-1613		19991201
HU 2002001613	A3	20030328			
AU 755202	B2	20021205	AU 2000-17491		19991201
CN 1129582	B	20031203	CN 1999-813902		19991201
NZ 510987	A	20040227	NZ 1999-510987		19991201
RU 2240998	C2	20041127	RU 2001-115714		19991201
AT 354569	T	20070315	AT 1999-960636		19991201
ES 2281975	T3	20071001	ES 1999-960636		19991201
TW 495504	B	20020721	TW 1999-88121090		19991202
IN 2001MN00460	A	20050304	IN 2001-MN460		20010426
ZA 2001004455	A	20020530	ZA 2001-4455		20010530
NO 2001002739	A	20010601	NO 2001-2739		20010601
NO 318897	B1	20050518			
MX 2001PA05532	A	20011101	MX 2001-PA5532		20010601
PRIORITY APPLN. INFO.:			US 1998-111079P	P	19981204
			WO 1999-US28428	W	19991201

OTHER SOURCE(S): MARPAT 133:43452
GI



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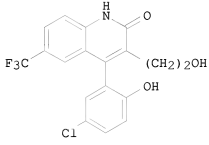


II

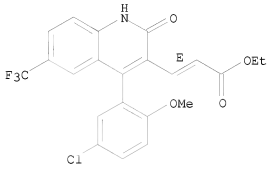
AB The title compds. (I) [wherein R and R1 = independently H or Me; R2, R3, and R4 = independently H, halogen, NO2, or CF3; R5 = Br, Cl, or NO2; R6 = H or F; R7 = Me, CRR1OH, CHO, C:NOH, COMe, or (un)substituted aryl; m = 0-1; n = 0-6] were prepared by cyclization and further reaction of 1-[2-(acylamino)phenyl]-1-phenylmethanone derivs. For example, 4-(5-chloro-2-hydroxyphenyl)-3-(2-hydroxyethyl)-6-(trifluoromethyl)-2(1H)-quinoline (II) was synthesized in a 5-step sequence starting with acylation of 1-[2-amino-5-(trifluoromethyl)phenyl]-1'-(5-chloro-2-methoxyphenyl)methanone (preparation given) with 3-carbomethoxypropionyl chloride (82%). Subsequent cyclization (100%), dehydration (78%), demethylation (86%), and reduction of the acid yielded II. II activated the cloned BK channel mSlo expressed in Xenopus oocytes, increasing whole cell outward (K+) BK-mediated currents > 200% at 20 μM. In an in vivo erectile function test on diabetic F-344 rats, II (0.1-1 mg/kg) significantly augmented intracavernous pressure/BP responses elicited by submaximal stimulation of the cavernous nerve. As BK channel openers, I are useful in the treatment of disorders which are responsive to the opening of the potassium channels, such as ischemia, stroke, convulsions, epilepsy, asthma, irritable bowel syndrome, migraine, traumatic brain injury, spinal cord injury, sexual dysfunction, and urinary incontinence.

IT 275375-54-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 3-substituted-4-arylquinolin-2-one potassium channel openers by cyclization and further reaction of 1-[2-(acylamino)phenyl]-1-phenylmethanone derivs.)

RN 275375-54-7 CA

CN 2-Propenoic acid, 3-[4-(5-chloro-2-methoxyphenyl)-1,2-dihydro-2-oxo-6-(trifluoromethyl)-3-quinolinyl]-, ethyl ester, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 132:122527 CA
TITLE: Process for the preparation of quinoline derivative and intermediate therefor
INVENTOR(S): Ohara, Yoshio; Suzuki, Mikio; Yanagawa, Yoshinobu; Takada, Yasutaka
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005213	A1	20000203	WO 1999-JP3923	19990722
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338334	A1	20000203	CA 1999-2338334	19990722
AU 9947992	A	20000214	AU 1999-47992	19990722
AU 746722	B2	20020502		
EP 1099694	A1	20010516	EP 1999-931484	19990722
EP 1099694	B1	20050817		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 509401	A	20020828	NZ 1999-509401	19990722
CN 1107670	B	20030507	CN 1999-809003	19990722
RU 2214402	C2	20031020	RU 2001-105200	19990722
AT 302190	T	20050915	AT 1999-931484	19990722
PT 1099694	T	20051031	PT 1999-931484	19990722
ES 2247813	T3	20060301	ES 1999-931484	19990722

SK 285675	B6	20070607	SK 2001-62		19990722
ZA 2001000525	A	20010801	ZA 2001-525		20010118
NO 2001000357	A	20010122	NO 2001-357		20010122
NO 317787	B1	20041213			
US 6335449	B1	20020101	US 2001-764994		20010123
MX 2001PA00890	A	20020604	MX 2001-PA890		20010123
PRIORITY APPLN. INFO.:			JP 1998-207911	A	19980723
			WO 1999-JP3923	W	19990722

OTHER SOURCE(S): CASREACT 132:122527

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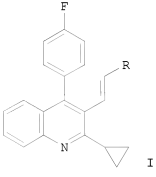

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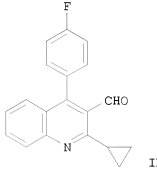


II

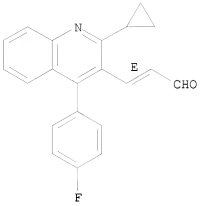
AB Claimed is a process for the preparation of 3-quinolinylpropenal derivative (I; R = CHO) through quinolylacrylonitrile I (R = cyano) which can be prepared by reacting quinolinealdehyde (II) with di-Et cyanomethyl phosphonate. I (R = CHO) is useful as an intermediate for a cholesterol-lowering agent (HMG-CoA reductase inhibitor) (III.1/2Ca). Thus, 400 g 20% aqueous NaOH was added dropwise to a mixture of II 199, di-Et cyanomethylphosphonate 136, and Aliquat 336 5.5 g in 960 g PhMe at 25-35° over 0.5-1 h and stirred at the same temperature for 1 h to give, after workup and recrystn. from hexane, 88% I (R = cyano). The latter nitrile (181 g) was dissolved in 1,812 mL PhMe and cooled to -10°, followed by adding a 1.02 M solution of diisobutylaluminum (664 mmol, 650 mL) at -10° to -5° over 1 h, and the resulting mixture was stirred at the same temperature for 1 h to give, after workup and recrystn. from a mixture of cyclohexane and n-hexane, 93% I (R = CHO).

IT 148901-68-2P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinolinylpropenal derivative by condensation of quinolinealdehyde derivative with di-Et cyanomethylphosphonate and reduction of quinolylacrylonitrile derivative)

RN 148901-68-2 CA

CN 2-Propenal, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-, (2E)- (CA INDEX NAME)

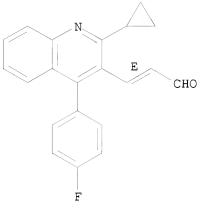
Double bond geometry as shown.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 132:93197 CA
TITLE: First systematic chiral syntheses of two pairs of enantiomers with 3,5-dihydroxyheptenoic acid chain, associated with a potent synthetic statin NK-104
AUTHOR(S): Suzuki, Mikio; Yanagawa, Yoshinobu; Iwasaki, Hiroshi; Kanda, Hiroyasu; Yanagihara, Kazufumi; Matsumoto, Hiroo; Ohara, Yoshio; Yazaki, Yukari; Sakoda, Ryozo
CORPORATE SOURCE: Central Research Institute, Nissan Chemical Industries Ltd., Chiba, 274-8507, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(20), 2977-2982
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:93197
AB All 4 enantiomers of the synthetic statin NK-104 were prepared The syn diol isomers (NK-104 and its enantiomer) were obtained efficiently by diastereomer resolution The anti diol isomers (3-epimer and 5-epimer) were prepared effectively by asym. aldol reaction followed by anti stereoselective reduction as key steps. Their purity detns. were effected by chiral HPLC anal.
IT 148901-68-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of the enantiomers of NK-104)
RN 148901-68-2 CA
CN 2-Propenal, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.

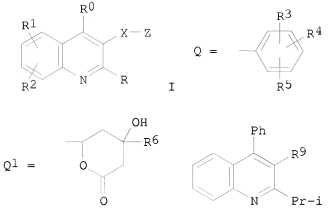


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 129:28109 CA
TITLE: Preparation of quinoline analogs of mevalonolactone and derivatives as anticholesteremics
INVENTOR(S): Wattanasin, Sompong
PATENT ASSIGNEE(S): Novartis Pharmaceuticals Corp., USA
SOURCE: U.S., 19 pp., Cont. of U.S. Ser. No. 318,773, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5753675	A	19980519	US 1990-498301	19900323
PRIORITY APPLN. INFO.:			US 1989-318773	B1 19890303

OTHER SOURCE(S): MARPAT 129:28109
GI



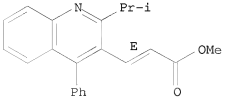
AB The title compds. [I; R, R0 = alkyl, cycloalkyl, Q; R1-R5 = H, alkyl, alkoxy, CF3, F, Cl, phenoxy, benzyloxy, OH; with provisos; X = (CH2)2, vinylene; Z = Y-CH2-CR6(OH)-CH2-COO-R7, Q1; Y = CO, CHOH, with provisos; R6 = H, alkyl; R7 = H, physiol. acceptable and hydrolyzable ester group,pharmaceutically acceptable cation], quinoline analogs of mevalonolactone, useful as anti-cholesterol synthesis agents, are prepared Thus, quinolinecarboxaldehyde II [R9 = CHO] (also prepared) was reacted with Ph3P:CH-CO2Me, the resulting II [R9 = CH:CH-CO2Me] was treated with DIBAL, the resulting II [R9 = CH:CH-CHO] was reacted with Et acetoacetate in the presence of NaH and BuLi, the resulting II [R9 = CH:CH-CH(OH)-CH2-CO-CH2-COOEt] was treated with BEt3 in THF followed by treatment with NaBH4 to give the title compound II [R9 = CH:CH-CH(OH)-CH2-CH(OH)-CH2-COOEt]. I [R1 = R2 = H, R = iso-Pr, R0 = p-fluorophenyl, X = vinylene, Z = (3R,5S)-CH(OH)-CH2-CH(OH)-CH2-COOEt] (also prepared) had an IC50 of 0.41 μmol in an in vitro microsomal assay of its inhibition on HMG-CoA reductase.

IT 207976-76-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinoline analogs of mevalonolactone and derivs. as anticholesteremics)

RN 207976-76-9 CA

CN 2-Propenoic acid, 3-[2-(1-methylethyl)-4-phenyl-3-quinolinyl]-, methyl ester, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 125:248102 CA
TITLE: Preparation of optically active 3-(silyloxy)-5-oxoheptenoic acid ester
INVENTOR(S): Harada, Katsumasa; Matsushita, Akio; Kawachi, Yasuhiro; Sasaki, Hiroshi
PATENT ASSIGNEE(S): Ube Kosan KK, Japan; Nissan Kagaku Kogyo KK; Nissan Chemical Industries, Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

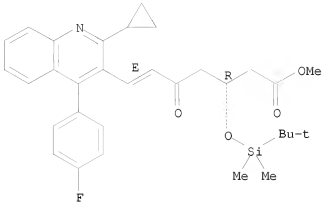
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08127585	A	19960521	JP 1994-276395	19941110
JP 3481325	B2	20031222		
PRIORITY APPLN. INFO.:			JP 1994-276395 A	19941110
			JP 1994-212960	19940906

OTHER SOURCE(S): CASREACT 125:248102
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title ester (I), useful as intermediate for pharmaceuticals, is prepared in high yields by an improved process. K2CO3 was added to a solution of aldehyde II and (R)-III (99% e.e) in 1:1 iso-PrOH-THF containing 0.63% H2O with stirring at room temperature to give 94% (3R,6E)-I of 99% e.e. Also used was MeOH-THF.
IT 182075-76-9P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of optically active 3-(silyloxy)-5-oxoheptenoic acid ester)
RN 182075-76-9 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-oxo-, methyl ester, (3R,6E)-(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L7 ANSWER 24 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 123:286068 CA
TITLE: Preparation of pyrimidine derivatives
INVENTOR(S): Okada, Tetsuo; Konoike, Toshiro
PATENT ASSIGNEE(S): Shionogi Seiyaku Kk, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07118233	A	19950509	JP 1993-261365	19931019
JP 3400038	B2	20030428		
PRIORITY APPLN. INFO.:			JP 1993-261365	19931019

OTHER SOURCE(S): CASREACT 123:286068; MARPAT 123:286068
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

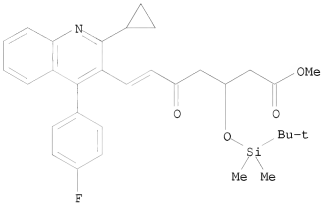
AB Pyrimidine derivs. I [R1 = (un)substituted alkyl, etc.; R2, R3 = H, (un)substituted alkyl, etc.; R4 = H, carboxy-protecting group; R5 = H, hydroxy-protecting group; X = N, etc.], useful as pharmaceutical intermediates, are prepared from pyrimidinecarboxaldehydes. Thus, a mixture of pyrimidine derivative II, phosphonate III (TBDMS = tert-butyldimethylsilyl), and potassium tert-butoxide in acetonitrile was stirred at room temperature for 30 min to give, after workup, 74% pyrimidine derivative IV.

IT 169196-10-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyrimidine derivs.)

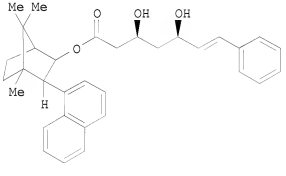
RN 169196-10-5 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-oxo-, methyl ester, (-)- (CA INDEX NAME)

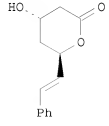
Rotation (-).
Double bond geometry unknown.



L7 ANSWER 25 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 123:285697 CA
TITLE: Stereoselective reduction of β,δ-diketo esters. A novel strategy for the synthesis of artificial HMG-CoA reductase inhibitors
AUTHOR(S): Hiyama, Tamejiro; Reddy, Guntoori Bhaskar; Minami, Tatsuya; Hanamoto, Takeshi
CORPORATE SOURCE: Sagami Chemical Research Center, Kanagawa, 229, Japan
SOURCE: Bulletin of the Chemical Society of Japan (1995), 68(1), 350-63
CODEN: BCSJA8; ISSN: 0009-2673
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 123:285697
GI



I



II

AB Condensation of N-methoxy-N-Me amides with acetoacetate dianions gave

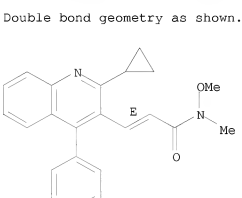
β,δ-diketo esters, which were selectively reduced with Et2BOMe-NaBH4 in THF/MeOH to give syn-β,δ-dihydroxy esters in one step. Similarly, the β,δ-diketo esters of the Taber's chiral alc. or its enantiomer resp. were reduced to give syn-β,δ-dihydroxy esters of moderate enantiomeric excess. Higher diastereoselective and enantioselectivity were achieved by reduction of the β,δ-diketo esters of Taber's chiral alc. or its enantiomer successively with diisobutylalane and with Et2BOMe-NaBH4. The resulting syn-diol esters were hydrolyzed and lactonized to give various types of β-hydroxy-δ-lactones commonly found in artificial HMG-CoA reductase inhibitors; pharmacol. test data were not shown. The precursor I was converted to the example compound [4S-[4α,6β(E)]]-tetrahydro-4-hydroxy-6-(2-phenylethenyl)-2H-pyran-2-one (II).

IT 141750-56-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of β-hydroxy-δ-lactones as HMG-CoA reductase inhibitors)

RN 141750-56-3 CA

CN 2-Propenamide, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-N-methoxy-N-methyl-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



L7 ANSWER 26 OF 36 CA COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 123:168993 CA

TITLE: Optically active β-aminoalkoxyborane complex as asymmetric reducing agent

INVENTOR(S): Kashihara, Hiroshi; Suzuki, Mikio; Ohara, Yoshio

PATENT ASSIGNEE(S): Nissan Chemical Industries Ltd., Japan

SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9417079	A1	19940804	WO 1994-JP56	19940117

W: AU, CA, CN, CZ, FI, HU, KR, NO, NZ, RO, RU, UA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

JP	06329679	A	19941129	JP 1993-332498	19931227
TW	383309	B	20000301	TW 1994-83100279	19940114
CA	2153695	A1	19940804	CA 1994-2153695	19940117
AU	9458431	A	19940815	AU 1994-58431	19940117
AU	678427	B2	19970529		
EP	680484	A1	19951108	EP 1994-904332	19940117
EP	680484	B1	19980819		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

CN	1116850	A	19960214	CN 1994-190966	19940117
CN	1047173	B	19991208		
HU	72018	A2	19960328	HU 1995-2184	19940117
HU	217182	B	19991228		
AT	169921	T	19980915	AT 1994-904332	19940117
RU	2126412	C1	19990220	RU 1995-115845	19940117
ZA	9400383	A	19940907	ZA 1994-383	19940119
IL	108387	A	20000629	IL 1994-108387	19940120
NO	9502870	A	19950919	NO 1995-2870	19950719
NO	305602	B1	19990628		
US	5663348	A	19970902	US 1995-481505	19950719
US	5767277	A	19980616	US 1997-779621	19970107
US	5739347	A	19980414	US 1997-848173	19970429
US	5786485	A	19980728	US 1997-848172	19970429
US	5808098	A	19980915	US 1997-848169	19970429
US	5852221	A	19981222	US 1997-848174	19970429
NO	9805016	A	19950919	NO 1998-5016	19981028
CN	1234392	A	19991110	CN 1999-105088	19990409

PRIORITY APPLN. INFO.:	JP 1993-7827	A	19930120
	JP 1993-66825	A	19930325
	WO 1994-JP56	W	19940117
	US 1995-481505	A3	19950719

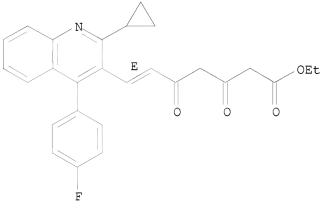
OTHER SOURCE(S): CASREACT 123:168993; MARPAT 123:168993
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Optically active β-aminoalkoxyborane complexes are disclosed, specifically I [R1 = C1-C8 alkyl, C3-C7 cycloalkyl, C7-C11 aralkyl or C6-C10 aryl; R2 = H, C1-C8 alkyl, C3-C7 cycloalkyl or C7-C11 aralkyl; or R1R2 = (CH2)n wherein n = 3 or 4; Ar = naphthyl, anthryl or phenanthryl, which may be substituted by 1-3 substituents selected from halo, nitro, C1-C6 alkyl, C3-C7 cycloalkyl, C2-C6 alkenyl or alkynyl, C7-C11 aralkyl, C6-C10 aryl, C1-C6 alkoxy, and styrene polymer substituents]. The complexes are useful for reducing carbonyl compds. to optically active alcs., and especially for reducing 1,3-dicarbonyl compds. to optically active 1,3-syn-diols. For example, reduction of proline Et ester with LiAlH4 to give (S)-prolinol, cyclocondensation of this with β-naphthaldehyde to give an oxazolidine derivative (quant.), reduction of this with NaBH4 to give an amino alc. (quant.), and reaction of the latter with BH3.THF (quant.), gave the (S)-isomeric complex II. Reduction of diketo ester III using II and Et2BOMe in THF at 20° gave the (3S,5R)-syn-diol IV in 53% yield and 100% enantiomeric excess (ee). In contrast, several similar known borane

complexes gave 28-78% yield but only 6-23% ee.
IT 166803-31-2P, (E)-Ethyl 7-[2-cyclopropyl-4-(p-fluorophenyl)quinolin-3-yl]-3,5-dioxo-6-heptenoate
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reduction substrate; preparation of optically active β-aminoalkoxyborane complexes for asym. reduction of (di)carbonyl compds.)
RN 166803-31-2 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, ethyl ester, (6E)- (CA INDEX NAME)

Double bond geometry as shown.

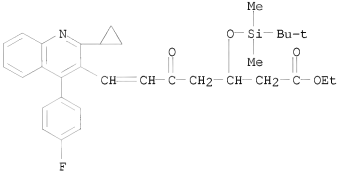


L7 ANSWER 27 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 121:179869 CA
TITLE: preparation of 6-phosphinylhexanoic acid derivatives
INVENTOR(S): Sakota, Ryozo; Obara, Yoshio; Suzuki, Mikio; Iwasaki, Hiroshi
PATENT ASSIGNEE(S): Nissan Chemical Ind Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06107673	A	19940419	JP 1992-288444	19921027
PRIORITY APPLN. INFO.:			JP 1992-215132	A1 19920812

OTHER SOURCE(S): MARPAT 121:179869
AB R1R2P(O)CH2COCH2CR3(OR4)CH2CO2Z [I; R1, R2 = H, C1-8 alkyl, C2-6 alkynyl, alkynyl, C3-7 cycloalkyl, cycloalkenyl, etc.; R3 = H, C1-3 alkyl; R4 = H, protecting group; Z = OH, C1-8 alkoxy, (un)substituted aryloxy, (un)substituted amino, etc.], useful as intermediates for HMG-CoA reductase inhibitors, are prepared A solution of Li diisopropylamide in THF-hexane was added to a solution of 11.96 g Ph2P(O)Me and 11.96 g di-Et 3-hydroxyglutarate in THF with stirring at -70° under N, followed by aqueous NH4Cl, to give 8.21 g I (R1 = R2 = Ph, R3 = R4 = H, Z = OEt).
IT 157684-62-3P

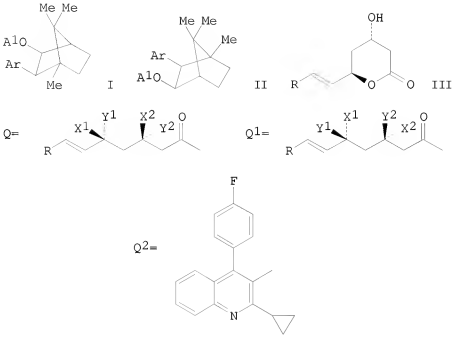
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for HMG-CoA reductase inhibitors)
RN 157684-62-3 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-oxo-, ethyl ester (CA INDEX NAME)



L7 ANSWER 28 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 121:35341 CA
TITLE: Preparation of optically active β,δ-diketo acid derivatives
INVENTOR(S): Hyama, Tamejiro; Minami, Tatsuya; Guntoori, Basukaaru Redei; Sakota, Ryozo; Arai, Kazutaka; Obara, Yoshio; Suzuki, Mikio
PATENT ASSIGNEE(S): Sagami Chem Res, Japan; Nissan Chemical Ind Ltd
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06025092	A	19940201	JP 1991-291586	19911107
PRIORITY APPLN. INFO.:			JP 1991-291586	19911107

OTHER SOURCE(S): CASREACT 121:35341; MARPAT 121:35341
GI

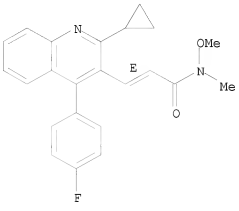


AB 2-Exo-(hetero)arylheptenoyloxy-3-exo-aryl-4,7,7-trimethylbicyclo[2.2.1]heptane derivs. [I; A1 = (un)substituted (hetero)aryl or vinyl; Ar = condensed aryl; X1, Y1 = H, OH or X1Y1 = O; X2, Y2 = H, OH or X2Y2 = O] and enantiomers thereof are prepared by treatment of acetoacetate derivs. I (A1 = MeCOCH2CO) with a base to generate a dianion followed by condensation with N-alkoxyamides trans-RCH:CHCONR1OR2 (Ar = same as above; R1, R2 = C1-4 linear or branched alkyl) and stereoselective reduction of the resulting β,δ-diketo acid derivs. I (A1 = trans-RCH:CHCOCH2COCH2CO). These derivs. I are useful as intermediates for 7-(R-substituted)-(E,3R,5S)-3,5-dihydroxy-6-heptenoic acid 1,5-lactones, hypocholesteremics, having hydroxymethylglutaryl-CoA (HMG-CoA) reductase-inhibitory activity. Thus, acetoacetate ester II (Ar = 2-naphthyl, A1 = MeCOCH2CO) was treated with NaH in THF at 0° followed by addition of BuLi/hexane at 0° and cooling to -78° and a solution of a N-methoxy-N-methylamide trans-RCH:CHCONMeOMe (R = Q2) (preparation given) in THF was added to give, after stirring at -78° to 0° for 3 h, 48% quinolyldioxoheptenoic acid derivative I (A1 = trans-RCH:CHCOCH2COCH2CO, R = Q2, Ar = 2-naphthyl). The latter compound was reduced by NaBH4 in the presence of Et2BOMe in THF/MeOH at -78° to room temperature to give quinolyldihydroxyheptenoic acid ester 90% (A1 = Q1, R = Q2, X1 = X2 = OH, Y1 = Y2 = H, Ar = 2-naphthyl) which was saponified with aqueous NaOH in MeOH and lactonized by refluxing in toluene to give lactone III (R = Q2) of 58% e.e. as a 77:23 mixture of trans/cis isomers.

IT 141750-56-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation of, with trimethylnaphthylbicycloheptyl acetoacetate)

RN 141750-56-3 CA
CN 2-Propenamide, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-N-methoxy-N-methyl-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.

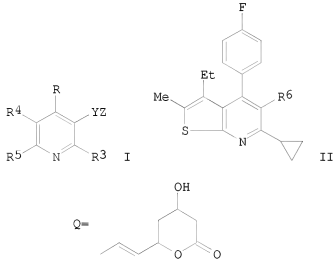


L7 ANSWER 29 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 119:117112 CA
TITLE: Preparation of (heterocyclylvinyl)mevalonic lactone analogs as antiatherosclerotics
INVENTOR(S): Saito, Yasushi; Kitahara, Masaki; Sakashita, Mitsuaki; Toyoda, Kyomi; Shibazaki, Toshie
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan; Kowa Co., Ltd.
SOURCE: Eur. Pat. Appl., 64 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 535548	A1	19930407	EP 1992-116417	19920924
EP 535548	B1	20011121		
R: AT, BE, CH, DE, DK, FR, GB, IE, IT, LI, LU, NL, SE				
JP 06329540	A	19941129	JP 1991-257870	19911004
JP 3130342	B2	20010131		
AT 209035	T	20011215	AT 1992-116417	19920924
AU 9226012	A	19930408	AU 1992-26012	19920928
AU 652669	B2	19940901		
NZ 244555	A	20000623	NZ 1992-244555	19920930
US 6162798	A	20001219	US 1992-953716	19920930
NO 9203858	A	19930405	NO 1992-3858	19921002
NO 302452	B1	19980309		
CA 2079706	A1	19930415	CA 1992-2079706	19921002
CA 2079706	C	20040330		
HU 62794	A2	19930628	HU 1992-3138	19921002
HU 214624	B	19980428		
CZ 281786	B6	19970115	CZ 1992-3027	19921002

RU 2114620	C1	19980710	RU 1992-5052949		19921002
SK 279277	B6	19980909	SK 1992-3027		19921002
PRIORITY APPLN. INFO.:			JP 1991-257870	A	19911004
OTHER SOURCE(S):	MARPAT 119:117112				

GI



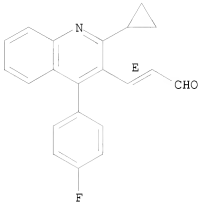
AB Title compds. [I; R = substituted-Ph; R3 = H, (cyclo)alkyl, (cyclo)alkenyl, (substituted)Ph, etc.; R4R5 = atoms to complete a fused benzene or 5- or 6-membered heteroaryl ring; Y = CH2, CH2CH2, CH:CH, etc.; Z = 4-hydroxy-2-oxo- or 2,4-dioxo-6-tetrahydropyranyl, QCH2WCH2CO2R12, etc.; Q = CO, CH(OH), etc.; R12 = H, ammonium, physiol. labile ester residue, etc.; W = CO, CH(OH), etc.], inhibitors of atherosclerotic intimal thickening, were prepared Thus, thienopyridinecarboxyaldehyde II (R6 = CHO) was condensed with Bu3SnC(OEt):CH2 and the product hydrolyzed to give II [R6 = (E)-CH:CHCHO] which was condensed with MeCOCH2CO2Et to give, in 3 addnl. steps, II (R6 = oxopyranylvinyl group Q). The latter gave 100% inhibition of smooth muscle cell proliferation at 10-6 M (intimal) and 10-5 M (medial) in vitro.

IT 148901-68-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of antiatherosclerotic)

RN 148901-68-2 CA

CN 2-Propenal, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-, (2E)- (CA INDEX NAME)

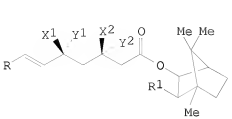
Double bond geometry as shown.



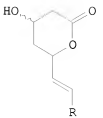
L7 ANSWER 30 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 117:7804 CA
ORIGINAL REFERENCE NO.: 117:1575a,1578a
TITLE: Optically active esters of 7-substituted 3,5-difunctionalized 6-heptenoic acids
INVENTOR(S): Hiyama, Tamejiro; Minami, Tatsuya; Hanamoto, Takeshi; Reddy, Guntoori Bhaskar
PATENT ASSIGNEE(S): Sagami Chemical Research Center, Japan
SOURCE: Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 475627	A1	19920318	EP 1991-307837	19910828
EP 475627	B1	19941019		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05004943	A	19930114	JP 1991-214148	19910801
US 5276154	A	19940104	US 1991-748076	19910821
HU 58267	A2	19920228	HU 1991-2818	19910829
HU 209583	B	19940829		
CA 2050266	A1	19920301	CA 1991-2050266	19910829
US 5369109	A	19941129	US 1993-77454	19930617
PRIORITY APPLN. INFO.:			JP 1990-226741 A	19900830
			JP 1991-214148 A	19910801
			US 1991-748076 A3	19910821

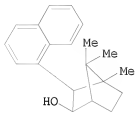
OTHER SOURCE(S): MARPAT 117:7804
GI



I



II



III

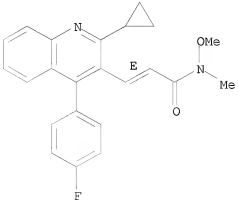
AB Title esters I [R = (un)substituted aromatic, heteroarom., substituted vinyl; R1 = condensed aromatic; X1 = H, Y1 = OH, X1 = OH, Y1 = H, X1Y1 = O; X2 = H, Y2 = OH, X2 = OH, Y2 = H, X2Y2 = O] were prepared as intermediates for the HMG-CoA reductase-inhibiting heptenolides II. Thus, (-)-camphor was converted to the alc. III in 5 steps. III was converted to its acetoacetate and heated with (E)-PhCH:CHCONMeOMe to give I (R = Ph, R1 = 1-naphthyl, X1Y1, X2Y2 = O). The latter compound was reduced by MeOBEt2 to I (R = Ph, R1 = 1-naphthyl, X1, X2 = H, Y1, Y2 = OH) which was hydrolyzed to (3S,5R)-II (R = Ph).

IT 141750-56-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with trimethyl(naphthyl)bicycloheptyl acetoacetate)

RN 141750-56-3 CA

CN 2-Propenamide, 3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-N-methoxy-N-methyl-, (2E)- (CA INDEX NAME)

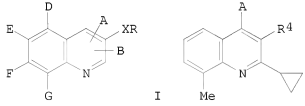
Double bond geometry as shown.



L7 ANSWER 31 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 114:82195 CA
ORIGINAL REFERENCE NO.: 114:14049a,14052a
TITLE: Preparation of 5-[3-(quinolinyl)vinyl- or ethyl]mevalonates as HMG-CoA reductase inhibitors
INVENTOR(S): Philipps, Thomas; Angerbauer, Rolf; Fey, Peter; Huebsch, Walter; Bischoff, Hilmar; Petzinna, Dieter; Schmidt, Delf
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 28 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

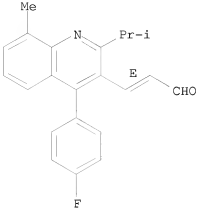
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3905908	A1	19900906	DE 1989-3905908	19890225
PRIORITY APPLN. INFO.:			DE 1989-3905908	19890225

OTHER SOURCE(S): CASREACT 114:82195; MARPAT 114:82195
GI

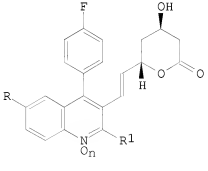


AB The title compds. [I; A = (un)substituted heterocyclyl, aryl, alkyl; B = cycloalkyl, (un)substituted alkyl, aryl; D = H, alkyl; E, F, G = H, halo, alkyl; R = CH(OH)CH2CR1(OH)CH2CO2R2 or δ-lactone form thereof; R1 = H, alkyl; R2 = H, alkyl, aryl, cation; X = CH2CH2, CH:CH] were prepared Thus, 2-amino-4'-fluoro-3-methylbenzophenone (preparation given) was cyclocondensed with R3COCH2CO2Me (R3 = cyclopropyl) to give quinolinecarboxylate II (A = 4-FC6H4)(III; R4 = CO2Me) which was converted in 2 steps to III (R4 = CHO). The latter was condensed with (EtO)2P(O)CH:CHNHR5 (R5 = cyclohexyl) and the product [III; (E)-CH:CHCHO] condensed with MeCOCH2CO2Me to give, after reduction, III [R4 = (E)-CH:CHCH(OH)CH2CH(OH)CH2CO2Me] which was 53 times as potent as mevinolin in inhibition of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase in vitro.
IT 131775-24-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of HMG-CoA reductase inhibitors)
RN 131775-24-1 CA
CN 2-Propenal, 3-[4-(4-fluorophenyl)-8-methyl-2-(1-methylethyl)-3-quinolinyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L7 ANSWER 32 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 114:61895 CA
ORIGINAL REFERENCE NO.: 114:10611a,10614a
TITLE: Inhibitors of cholesterol biosynthesis. 4. trans-6-[2-(Substituted-quinolinyl)ethenyl/ethyl]tetrahydro-4-hydroxy-2H-pyran-2-ones, a novel series of HMG-CoA reductase inhibitors
AUTHOR(S): Sliskovic, D. R.; Picard, J. A.; Roark, W. H.; Roth, B. D.; Ferguson, E.; Krause, B. R.; Newton, R. S.; Sekerke, C.; Shaw, M. K.
CORPORATE SOURCE: Parke-Davis Pharm. Res. Div., Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SOURCE: Journal of Medicinal Chemistry (1991), 34(1), 367-73
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:61895
GI



I

AB A series of substituted quinoline mevalonolactones I (n = 0, R = H, Cl, F, OMe, R1 = CHMe2; R = Cl, R1 = Me; R = H, R1 = NMe2; n = 1, R = F, R1 = NMe2) were prepared and evaluated for their ability to inhibit the enzyme

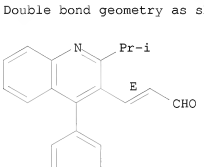
HMG-CoA reductase both in vitro and in vivo cholesterol biosynthesis. Since previous studies suggested that the 4-(4-fluorophenyl) and 2-(1-methylethyl) substituents afforded optimum potency, attention was focused on variations at position 6 of the quinoline ring. Biol. evaluation of a small number of analogs bearing a variety of 6-substituents showed that modification at this position had little effect on potency. I (n = 0, R = Cl, OMe, R1 = CHMe2; n = 1, R = F, R1 = CHMe2) showed comparable potency to compactin and mevinolin in both the in vitro and in vivo assays.

IT 121659-68-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and condensation reaction of, with acetoacetate sodium salt)

RN 121659-68-5 CA

CN 2-Propenal, 3-[4-(4-fluorophenyl)-2-(1-methylethyl)-3-quinolinyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L7 ANSWER 33 OF 36 CA COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 113:191184 CA

ORIGINAL REFERENCE NO.: 113:32361a,32364a

TITLE: Preparation of 6-[2-[2-(substituted amino)-3-quinolinyl]ethenyl- and -ethyl]tetrahydro-4-hydroxypyran-2-one inhibitors of cholesterol biosynthesis

INVENTOR(S): Picard, Joseph A.; Sliskovic, Drago R.

PATENT ASSIGNEE(S): Warner-Lambert Co., USA

SOURCE: U.S., 12 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

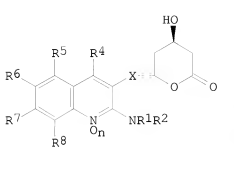
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4923861	A	19900508	US 1989-307442	19890207

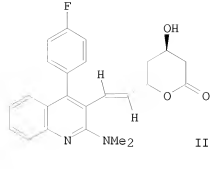
PRIORITY APPLN. INFO.: US 1989-307442 19890207

OTHER SOURCE(S): CASREACT 113:191184; MARPAT 113:191184

GI



I



II

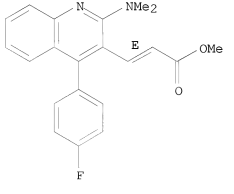
AB The title compds. [I; X = CH2, CH:CH; R1, R2 = H, alkyl; R1R2N = (O-, S-, imino-containing) ring; R4 = H, alkyl, CF3, cyclopropyl, cyclohexyl(methyl), (substituted) PhCH2, pyrazinyl, pyridinyl, pyrimidinyl; R5, R6, R7, R8 = alkyl, CF3, cyclopropyl, F, Cl, Br, OH, alkoxy, cyano, NO2, (acetyl)amino, aminomethyl, (substituted) Ph, PhCH2; n = 0, 1] and their hydroxyacid (ester) forms, were prepared Thus, quinolinylethenylpyranone II was prepared in 13 steps starting from EtO2CCH2COCl and 2-aminophenyl-4-fluorophenyl ketone via selected intermediates Et 4-(4-fluorophenyl)-1,2-dihydro-2-oxo-3-quinolinecarboxylate, 2-chloro-4-(4-fluorophenyl)-3-quinolinecarboxaldehyde, Me (E)-3-[2-(dimethylamino)-4-(4-fluorophenyl)-3-quinolinyl]-2-propenoate, and Et (E)-7-[2-(dimethylamino)-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-6-heptenoate. II in rats gave 52% AICS (acute inhibition of cholesterol screen) inhibition (dose not given).

IT 130048-12-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for quinolinylethenylhydroxypyranone HMG-CoA reductase inhibitor)

RN 130048-12-3 CA

CN 2-Propenoic acid, 3-[2-(dimethylamino)-4-(4-fluorophenyl)-3-quinolinyl]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L7 ANSWER 34 OF 36 CA COPYRIGHT 2008 ACS on STN

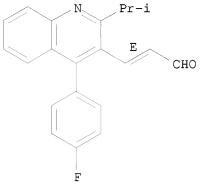
ACCESSION NUMBER: 111:134010 CA
ORIGINAL REFERENCE NO.: 111:22431a,22434a
TITLE: Quinolinylheptenoic acid derivatives as anticholesteremics, their preparation, and formulations containing them
INVENTOR(S): Fujikawa, Yoshihiro; Suzuki, Mikio; Iwasaki, Hiroshi; Sakashita, Mitsuaki; Kitahara, Masaki
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 304063	A2	19890222	EP 1988-113448		19880818
EP 304063	A3	19901003			
EP 304063	B1	19941130			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP 01279866	A	19891110	JP 1988-193606		19880803
JP 2569746	B2	19970108			
CA 1336714	C	19950815	CA 1988-574999		19880817
ES 2067460	T3	19950401	ES 1988-113448		19880818
US 5011930	A	19910430	US 1990-483720		19900223
US 5102888	A	19920407	US 1990-483724		19900223
US 5185328	A	19930209	US 1990-483829		19900223
US 5872130	A	19990216	US 1990-631092		19901219
US 5856336	A	19990105	US 1992-883398		19920515
US 5854259	A	19981229	US 1992-978884		19921119
PRIORITY APPLN. INFO.:			JP 1987-207224	A	19870820
			JP 1988-15585	A	19880126
			JP 1988-193606	A	19880803
			US 1988-233752	A3	19880819
			US 1990-631092	A3	19901219
			US 1992-883398	A3	19920515

OTHER SOURCE(S): CASREACT 111:134010; MARPAT 111:134010
GI For diagram(s), see printed CA Issue.
AB The title compds. I [R1-R4, R6 = H, C1-6 alkyl, C3-6 cycloalkyl, C1-3 alkoxy, etc.; or R1 and R2, R3 and R4 may form CH:CHCH:CH, etc.; Y = CH2, CH2CH2, CH:CH, CH2CH:CH, CH:CHCH2; Z = QCH2WCH2CO2R12, Q1, etc.; Q = C(O), CH(OH), etc.; W = C(O), C(R11)(OH), etc.; R11 = H, C1-6 alkyl; R12 = H, R14; R14 = physiol. hydrolyzable alkyl, M; M = NH4, Na, K, etc.; R5 = H, C1-6 alkyl, C2-3 alkenyl, C3-6 cycloalkyl, etc.], useful as cholesterol biosynthesis inhibitors, were prepared Reduction of Et (E)-7-[4'-(4''-fluorophenyl)-2'-(1'''-methylethyl)quinolin-3'-yl]-5-hydroxy-3-oxohept-6-enoate (preparation given) with NaBH4, followed by saponification in 0.5N NaOH, gave (E)-3,5-dihydroxy-7-[4'-(4''-fluorophenyl)-2'-(1'''-methylethyl)-quinolin-3'-yl]-hept-6-enoic acid Na salt (II). II exhibited an IC50 of 1.0 + 10-8M against cholesterol biosynthesis from acetate in vitro. A capsule formulation containing II 1, lactose 3.5, cellulose 10, Mg stearate 0.5 g is given.
IT 121659-68-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of cholesterol biosynthesis inhibitor)
RN 121659-68-5 CA
CN 2-Propenal, 3-[4-(4-fluorophenyl)-2-(1-methylethyl)-3-quinolinyl]-, (E)- (9CI) (CA INDEX NAME)

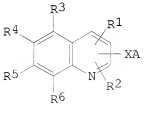
Double bond geometry as shown.



L7 ANSWER 35 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 110:38910 CA
ORIGINAL REFERENCE NO.: 110:6479a,6482a
TITLE: Preparation and formulation of 6-substituted quinolinylethyl- and -ethenyltetrahydro-4-hydroxypyran-2-ones as inhibitors of cholesterol biosynthesis
INVENTOR(S): Picard, Joseph A.; Roth, Bruce D.; Sliskovic, Drago R.
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4761419	A	19880802	US 1987-129516	19871207

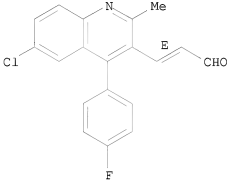
PRIORITY APPLN. INFO.: US 1987-129516 19871207
OTHER SOURCE(S): CASREACT 110:38910; MARPAT 110:38910
GI



I

AB Title compds. I [A = 4-hydroxypyran-2-onyl; X = CH2CH2, CH:CH; R1, R2 = H, Cl-6 alkyl, F3C, cyclopropyl, cyclohexyl, cyclohexylmethyl, (un)substituted Ph, (un)substituted PhCH2; R3, R4, R5, R6 = Br, Cl, F, HO, cyclopropyl, Cl-6 alkoxy, NC, H2N, O2N, AcNH, (un)substituted Ph, etc.] and their salts, were prepared [R,S(E)]-7-[6-Chloro-4-(4-fluorophenyl)-2-methyl-3-quinolinyl]-3,5-dihydroxy-6-heptenoic acid prepared in 10 steps was dehydrated to give [4α,6β(E)-I (R1 = 4-FC6H4, R2 = Me, R3, R6 = H, R4 = Cl, X = CH:CH) (II). Inhibition of sterol synthesis over 1 h expressed as IC50 for II was 0.35 μM/L and for [4α,6β(E)]-I (R1 = 4-FC6H4, R2 = Me2CH, R3, R5, R6 = H, R4 = Cl, X = CH:CH) was 0.032 μM/L.
IT 118314-80-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and aldol condensation of)
RN 118314-80-0 CA
CN 2-Propenal, 3-[6-chloro-4-(4-fluorophenyl)-2-methyl-3-quinolinyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



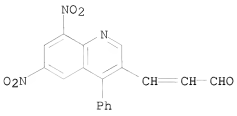
L7 ANSWER 36 OF 36 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 44:3113 CA
ORIGINAL REFERENCE NO.: 44:630b-i
TITLE: Novel synthesis of some quinoline derivatives
AUTHOR(S): Allan, Douglas; Loudon, James D.
SOURCE: Journal of the Chemical Society (1949) 821-5
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB 2,3-HO(O2N)C6H3CHO (I) (0.5 g.) and 0.6 g. p-MeC6H4SO2Cl (II) in 25 cc. hot H2O, treated with 0.32 g. Na2CO3 and refluxed 1 hr., give the p-toluenesulfonate (III) of I, m. 131°. I (5 g.) in 15 cc. C5H5N, treated (temperature below 27°) with 6 g. II, kept 12 hrs. at room temperature, and poured into dilute HCl and ice, give 3.3 g. III; the filtrate, neutralized with dilute NaOH, gives 2.3 g. 8-nitro-3-quinolineacraldehyde (IV), m. 201-2°; oxime, golden yellow, m. 250° (decomposition); phenylhydrazone, orange, m. 205°; diacetate, m. 136-7°. If the above C5H5N solution is warmed a few min. at 40°, the yield of III is decreased and that of IV correspondingly increased, but the IV is less pure. IV and Br in warm AcOH give α,β-dibromo-8-nitro-3-

quinolinepropionaldehyde, yellow, m. 220° (decomposition); shaken with aqueous Na2CO3 or boiled with AcOH, it yields α-bromo-8-nitro-3-quinolineacraldehyde (V), m. 183° (diacetate, m. 150-1°). Careful heating (1 hr.) of IV in HNO3 (d. 1.42) gives 8-nitro-3-quinolinecarboxylic acid (VI), m. 285° (decomposition); sublimation at its m.p. gives unchanged VI and 8-nitroquinoline. VI also results from V. 2,5-HO(O2N) C6H3CHO (VII) (2 g.), 2.4 g. II, and 10 cc. PhNMe2, heated 1 hr. at 100°, give the p-toluenesulfonate (VIII) of VII, m. 97-8°; 30 g. II, added to 25 g. VII in 25 cc. warm C5H5N and heated a few min. at 100°, gives 67% VIII. VIII (4 g.) in 4 cc. anhydrous C5H5N and 3 cc. C6H6, refluxed 2 hrs., give 1-(4-nitro-2-formylphenyl)pyridinium p-toluenesulfonate (IX), m. 215-16°. The aqueous filtrate from VIII, the aqueous solution of IX, or the solution obtained on heating 2,5-Cl(O2N)C6H3CHO or VIII 2 hrs. with C5H5N at 100° and pouring into cold dilute HCl, treated dropwise with 10% NaOH until no further color change occurs, and the mixture kept 30 min. and acidified, gives 6-nitro-3-quinolineacraldehyde, pale yellow, m. 247°; phenylhydrazone, orange-red, m. 226-8° (decomposition); diacetate, m. 188°; oxidation with HNO3 gives 6-nitro-4-quinolinecarboxylic acid, m. 300° (decomposition). II (1 g.), added to a suspension of 1 g. 2,3,5-HO(O2N)2C6H2CHO in 10 cc. C5H5N, shaken 30 min. at room temperature, allowed to stand several hrs., poured into dilute HCl, made alkaline with Na2CO3, and warmed to 60°, gives 6,8-dinitro-3-quinolineacraldehyde (X), m. 241° [phenylhydrazone, dark red, m. 245° (decomposition); diacetate, m. 177-8°]. X yields a rather unstable di-Br derivative [m. 225° (decomposition)] which with cold dilute Na2CO3 gives the α-Br derivative of X, m. 238° (decomposition); oxidation of X gives 6,8-dinitro-3-quinolinecarboxylic acid, with 0.5 mol. H2O, m. 301-2° (decomposition). 2,3,5-Cl(O2N)2C6H2Bz (XI) (5 g.) in 15 cc. C5H5N, heated 30 min. at 100°, added to dilute HCl, and slowly treated with dilute NaOH until no further color change occurs, gives 6,8-dinitro-4-phenyl-3-quinolineacraldehyde, straw-color, m. 243-4°; it results also from XI, II, and C5H5N. 2-HOC6H4CHO (20 g.) in 100 cc. AcOH, treated with 30 g. HNO3 (d. 1.52) (temperature below 12°), and the mixture allowed to warm to 50-5°, poured onto ice, and distilled with steam, gives 4-5 g. of the 5-NO2 derivative; the residue yields 0.5 g. of the 3-NO2 derivative (XII); a mixture (4 g.) of the 2 isomers results on C6H6 extraction of the steam distillate; a di-NO2 derivative could not be obtained. The p-toluenesulfonate of XII, purple, m. 113-15°; that of the 5-NO2 derivative m. 93-4°; these derivs. give only traces of compds., apparently of a different type from those described above.

IT 860205-05-6P, 3-Quinolineacrolein, 6,8-dinitro-4-phenyl-
RL: PREP (Preparation)
(preparation of)

RN 860205-05-6 CA

CN 2-Propenal, 3-(6,8-dinitro-4-phenyl-3-quinolinyl)- (CA INDEX NAME)

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     FILE 'REGISTRY' ENTERED AT 11:18:15 ON 30 APR 2008

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     APR 2008
L1                STRUCTURE UPLOADED
L2             14 S L1

     FILE 'CASREACT' ENTERED AT 11:20:52 ON 30 APR 2008
L3             12 S L1 FULL

     FILE 'REGISTRY' ENTERED AT 11:22:46 ON 30 APR 2008
L4                STRUCTURE UPLOADED
L5              3 S L4
L6             73 S L4 FULL

     FILE 'CA' ENTERED AT 11:23:06 ON 30 APR 2008
L7             36 S L6/P

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---Logging off of STN---


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Executing the logoff script...


=> LOG Y

STN INTERNATIONAL LOGOFF AT 11:23:34 ON 30 APR 2008
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